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Prevalence of risk factors for coronary artery disease in urban Indian population

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MANUSCRIPT

ABSTRACT

Objective: The objective of the study was to assess the prevalence of risk factors for coronary artery disease in urban Indian population.

Methods: The study population included subjects from a national level organisation situated in different parts of the country {Males (n=10642), Females (n=1966) aged 20 to 60 years} and comprised of various ethnic groups, staying in different environmental conditions. The recruitment was done across India in 14 states, 20 cities, and, one union territory. All the following individuals were subjected to detailed questionnaire, medical examinations and anthropometric measurements. Blood samples were collected for blood glucose and serum lipid profile estimation. Resting ECG was also recorded for these subjects. Results were analyzed by using appropriate statistical tools.

Results: The study revealed that the family history of premature CAD was present in 4.6% of the study population. The overall prevalence of Diabetes was 16% and out of 16% diabetics, 5.6% were freshly diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication. Hypertension was present in 21% of subjects. Prevalence of dyslipidemia was significantly high with 45.6% of study subjects having high total cholesterol/HDL ratio. 78.6% Subjects had 2 or more risk factors for CAD.

Conclusion: The present study demonstrates high prevalence of CAD risk factors in the Indian urban population. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors to manage individuals at high risk for future CAD.

STRENGTHS & LIMITATIONS OF THE STUDY

- Our study is the first of its type in India where population was covered across various cities in India. The study population included people of various ethnicities, age groups, and living in different parts of the country.
- There are very few studies across the world where such a large population were studied for the conventional risk factors of CAD.
- The history and clinical examination of the subjects were collected by qualified doctors who interviewed & examined each subject of the study. All the biochemical investigations were performed by the same team using similar kits and evaluation technique.
- The limitation of the study was that out of approximately 40000 working population of this organisation only 14500 gave informed consent to participate in the study. Out of these 14500 subjects data could be completed in 12608 subjects and was statistically analysed.
- Because of the limited resources in Phase I we could study and evaluate only the conventional coronary risk factors.

INTRODUCTION

Coronary Artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries. It is a leading cause of death in India, and its contribution to

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mortality is rising; deaths due to CAD are expected to double from 1985 to 2015¹. According to the reports of National Commission on Macroeconomics & Health, there would be 62 million patients with CAD in 2015 in India and of these 23 million would be patients younger than 40 years of age². The prevalence of classical cardiovascular (CV) risk factors (CVRFs) such as hypertension, dyslipidemia, obesity and diabetes varies widely between different countries, and shows some important secular trends. The conventional risk factors of CAD can be divided in non-modifiable and modifiable risk factors. The former include age, sex and family history while the latter include diabetes mellitus, smoking, dyslipidemia, hypertension and obesity. There is increasing incidence to believe that Asian Indians are at an increased risk of CAD, which cannot be attributed to the common risk factors. Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of the CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrated that Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI-1) and homocysteine levels³. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes⁴ i.e. changes in diet, physical inactivity, drug and alcohol intake etc, and increase in prevalence of diabetes mellitus. The prevalence of risk factors in a population determines the future burden on health care services and loss of productive years of a particular person. It is not only a health risk for that individual but overall burden on the economy. There are no large scale studies of adequate sample size to evaluate the prevalence rate, risk factor patterns and electrocardiographic changes in Indian populations. This study was planned to evaluate the future risk of CAD in a national level organization. The organization has offices across the entire country (Fig 1). So the study population included subjects from various ethnic groups, staying in varied environments and consuming different varieties of diet. To the best of our knowledge our study is the first such study carried out across India, where the employees are working all over India and belong to different ethnicity spread across the country.

Key words

CAD: coronary artery disease; **BP:** blood pressure; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure; **FPG:** fasting plasma glucose; **PPPG:** post-prandial plasma glucose; **BMI:** body mass index; **LDL-cholesterol:** low-density cholesterol; **HDL-cholesterol:** high density cholesterol; **CVRFs:** cardiovascular risk factors



Figure 1: The various labs in country where study was carried out

MATERIAL AND METHODS

Patient Population and Study Design

All the subjects were employees of one national level organisation. The subjects of both the sexes were recruited after written informed consent. They fall in the age groups ranging from 20 to 60 years. The recruitment was done across India in 14 states, 20 cities, and, one union territory namely, Delhi (Delhi), Karnataka(Bangalore, Mysore), Andhra Pradesh (Hyderabad, Vishakahapatnam), Maharashtra (Pune, Ambernath, Ahmednagar), Uttar Pradesh (Agra, Kanpur), Rajasthan (Jodhpur), Himachal Pradesh (Manali), Chandigarh, Uttrakhand (Dehradun, Mussourrie) ,Orissa (Chandipur), Assam (Tejpur), Jammu & Kashmir (Leh), Madhya Pradesh (Gwalior), Tamil Nadu(Chennai), Kerala (Kochi). The patient recruitment was initiated in 2009 and the phase I evaluation was completed in 2012.Of the initial 14,500 subjects sampled, a complete data of 12608 subjects could be collected.

Ethical Clearance

The study was approved by the Institutional Ethics Committee of Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi.

Inclusion criteria

- a. Employee of the particular organization
- b. Apparently healthy individual
- c. Age 20 – 60 years
- d. Both the sexes

Exclusion criterion

- a. Known case of coronary artery disease (CAD)

Assessment process

Participants were asked to attend the Health Center of their respective institution at 8:00 am after an overnight fast. They were asked to continue their medication if any, as usual. A detailed questionnaire

MANUSCRIPT

was applied by medical personnel prior to clinical measurements and blood collection. The questionnaire recorded information on demographic data, socio-economic and marital status, and several lifestyle factors namely tobacco, alcohol and caffeine consumption, physical activity, family history, disease history, medication use, and family history of premature CAD in first degree relatives (age <55 years in men & <65 years in women). In women, further data regarding reproductive and obstetrical history, oral contraception and hormonal replacement therapy was collected.

Anthropometry and clinical examination including blood pressure measurement was carried out. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5mm using a height gauge. Body mass index (BMI) was defined as weight in Kg/ (height in meters)².

Blood pressure (BP) and heart rate were measured on the left arm, with an appropriately sized cuff, after at least 10 minutes rest in the seated position using an automated BP instrument. The average of the last two measurements was used for analysis. The subjects diagnosed to have high BP for the first time were called again the next day for BP monitoring before labeling them as hypertensive. In addition, waist and hip circumferences were measured as recommended. Resting ECG was also obtained as a part of evaluation.

Blood samples were collected in the fasting state and 2 hours after 75 grams of oral glucose. Biochemical evaluation of the blood samples included complete blood count, Fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), lipid profile, and liver & kidney function tests. The clinical chemistry tests were performed on fresh blood samples using automatic analyser on the same day. Subjects whose FPG was ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl were diagnosed as fresh cases of Diabetes Mellitus. Other subjects with past history of DM and/or taking medication for the same were also considered as Diabetics.

In the evaluation of Lipid profile the value of Total cholesterol/HDL cholesterol ≥ 4.5 was considered abnormal. Known cases of dyslipidemia and/or those on medication for the same were also included in dyslipidemia risk factor.

The strength of the study is that each participant had one on one interaction with at least one of the project team doctors. Each questionnaire was scrutinised by the doctor. So this added value to the data. In most of the epidemiological studies usually paramedics collect the data.

Table no. 1. Definitions for different risk factors in the study

Risk factor	Definition
Hypertension	Systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) ≥ 90 mm Hg during the visit and/or presence of anti-hypertensive drug treatment and was considered as known if the

MANUSCRIPT

	subject was aware of this condition.
Diabetes Mellitus	FPG \geq 126 mg/dl and/or PPPG \geq 200 mg/dl at the time of investigations and/or presence of anti-diabetic drug treatment and was considered as known if the subject was aware of this condition.
Obesity	BMI \geq 30 kg/ m ²
Overweight	BMI \geq 25 kg/m ² .
Hypercholesterolemia	Total blood cholesterol \geq 200 mg/dl
Decreased High density lipoprotein(HDL) cholesterol	\leq 40mg/dl
Adverse total cholesterol/High density lipoprotein ratio (Dyslipidemia)	\geq 4.5
Age	>45 years in men; >55 years in women
Sex	Male sex
Family History of CAD	Premature CAD in first degree relatives (<55 years in men & <65 years in women)
Risk factors for CAD	age, sex, family history, diabetes mellitus, smoking, dyslipidemia, hypertension and obesity

Table no.2: Baseline characteristics of the study population (n=12,608)

Parameters ± SD	MALES (n=10642)	FEMALES (n=1966)	P value
Age	44.34±10.63	42.47±10.34	.000
Height	166.92±6.89	154.74±6.34	.000
Weight	69.36±10.69	62.24±11.30	.001
BMI	24.89±3.58	26.02±4.69	.001
Systolic BP	127.35±16.12	120.05±15.25	.000
Diastolic BP	81.08±10.04	77.05±9.60	.000
FPG	95.91±31.08	93.48±32.10	0.01
PPPG	135.44±56.31	131.86±54.47	.01
Total Cholesterol	186.11±40.56	181.69±36.62	.001
HDL	42.46±11.55	46.54±11.36	.001

Statistical Analysis

The final data was recorded on a predesigned Performa and managed in Microsoft access. The data analysis was performed using SPSS 20.0. The values of various parameters are presented as mean and SD (standard Deviation), in absolute numbers and as percentage. Comparison between male and female was done by t-test. Correlation statistics between various risk factors was also computed. Minimum Significance level was set at 0.05.

MANUSCRIPT

RESULTS

A total of 14,500 subjects were evaluated in the study. After informed consent, exclusion criteria, clinical & biochemical assessment, complete data of 12,608 cases (Males – 10,642

Females – 1,966) was available for final analysis. Mean age of males was 44.34 ± 10.63 & median age being 47.00 years. Mean age of females was 42.47 ± 10.34 and median age was 44.00 years. Baseline characteristics are shown in **Table no. 2**.

Different parameters considered for calculating the risk factors and their results are depicted in **Table no. 3**.

Family history of premature CAD was present in 4.6% of the study population. The history of CAD in first degree relatives in males was 4.4% and in females was 6% (P value<0.05).

The prevalence of smoking was significantly higher in the men (13.8%) than females (0.1%), p value<0.001.

Out of 12603 study subjects, 6002 (47.6%) had BMI $\geq 25 \text{ kg/m}^2$ with 4910(46.1%) males and 1092(55.5%) of females, P value<0.001. On further analysis it was observed that 39.46% males and 38.6% of females were overweight with BMI 25-30 kg/m^2 , P value<0.001. The mean BMI of the overweight males was 26.93 ± 1.31 and 27.35 ± 1.44 of females. Obesity with BMI $\geq 30 \text{ kg/m}^2$ was present in 6.6% of males with mean BMI of 32.78 ± 4 and 16.7% of females with mean BMI of 33.41 ± 3.74 , p value <0.05.

Overall prevalence of Diabetes was 16% in study population with no significant difference present in male (16.6%) and female (12.7%) subjects. Out of 16% diabetics, 5.6% were fresh diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication.

Out of 10642 male subjects, 2383 (22.4%) were found to have hypertension, whereas out of 1966 female subjects, 264 (13.4%) had high BP, p value<0.001. Overall prevalence of hypertension was 21% in the study subjects. Of these subjects only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study.

The prevalence of dyslipidemia in study population was significantly high with 45.6% of study subjects having high total cholesterol/HDL cholesterol ratio. 48.27% of male subjects and 31.4% females were found to have dyslipidemia (P value<0.001).

Total number of subjects having 2 or more than 2 risk factors for CAD was 9909 (78.6%). 9251 (86.9%) male subjects had 2 or more than 2 risk factors in comparison to 658 (33.46%) females. The most prevalent risk factor in men was dyslipidemia present in 48.27% of males followed by BMI>25 present in 46.1% of males. Whereas in women BMI>25 was most prevalent factor present in 55.5% of women, followed by dyslipidemia in 31.45%.

HDL correlated negatively with FPG, PPPG, and BMI. BMI had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose and total cholesterol. Total cholesterol had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose, BMI (**Table No. 4**).

Table no.3: Percentage (%) of Risk factors in study population (n=12608)

Parameters	Total (n=12608)	MALES (n=10642)	FEMALES (n=1966)	P value
Family H/O CAD	580(4.6%)	460(4.4%)	120(6%)	<.05
Smoking	1471(11.6%)	1469(13.8%)	2(0.1%)	<.001

MANUSCRIPT

BMI >25 kg/m ²	6002(47.6%)	4910(46.1%)	1092(55.5%)	
Mean(SD)		27.8 ±3.59	29.17± (3.66)	<.001
BMI 25-30 kg/m ²	4959(39.3%)	4200(39.46%)	759(38.6%)	
Mean(SD)		26.93± 1.31	27.35± 1.44	<.001
BMI ≥30 kg/m ²	1029(8.2%)	700(6.6%)	329(16.7%)	
Mean(SD)		32.78 ± 4.00	33.41± 3.74	<.05
Diabetes Mellitus	2016 (16%)	1766(16.6%)	250 (12.7%)	Ns
Hypertension	2647 (21%)	2383(22.4%)	264(13.4%)	<.001
Dyslipidemia	5755 (45.6%)	5137 (48.27%)	618 (31.4%)	<.001

Table No 4. Correlations by Pearson correlation (2 tailed); (n=12608)

Parameters	BP Systolic	BP Diastolic	FPG	PPPG	Serum Total Cholesterol	Serum HDL	BMI
BP systolic	1	.715(**)	.149(**)	.136(**)	.086(**)	-.011	.190(**)
BP Diastolic	.715(**)	1	.119(**)	.107(**)	.114(**)	-.011	.216(**)
FPG	.149(**)	.119(**)	1	.821(**)	.095(**)	-.054(**)	.099(**)
PPPG	.136(**)	.107(**)	.821(**)	1	.092(**)	-.042(**)	.117(**)
Serum Total Cholesterol	.086(**)	.114(**)	.095(**)	.092(**)	1	.000	.063(**)
Serum HDL Cholesterol	-.011	-.011	-.054(**)	-.042(**)	.000	1	-.068(**)
BMI	.190(**)	.216(**)	.099(**)	.117(**)	.063(**)	-.068(**)	1

** Correlation is significant at the 0.01 level (2-tailed).

Discussion

A rise in the prevalence of CAD in the early half of the twentieth century and a subsequent decline in the later half have been well documented in the western countries. However, the scenario has reversed in the developing countries especially in India with a steady escalation in the prevalence of CAD. The CAD burden of India is expected to double by the year 2020, making it the single largest cause of death and 2nd largest cause of disability.

MANUSCRIPT

The present study deals with finding the prevalence of the risk factors of the CAD, in a national level organization where people from different regions of India work. The employees were of both the sex and age group of 20-60. In the present population of the study, we found that approximately half of the population had dyslipidemia (45.6%) and BMI above 25kg/m² (47.6%). About one fifth of the study population was hypertensive (21%) and one sixth had Diabetes mellitus(16%). 78.6% of the study population had 2 or more than 2 CAD risk factors which indicates that there is a large population who in the near future will develop CAD.

The results of our study can be compared with the results of Jaipur Heart Watch-5 done by Rajeev Gupta et al on 739 subjects with 451 men and 288 women. In the study, overweight/obesity was present in 46.2% in males and 50.7% of females. Prevalence of Hypertension was 39.5% in males and 24.6% of females. Diabetes was present in 15.5% of males and 10.85 of females. 33% of the males and 32.7% of the females had high cholesterol levels.

Similar results are shown by a study done by Prabhakaran D et al among men working in an industry of Northern India. It showed high serum total cholesterol/HDL ratio in 62%, overweight in 47%, hypertension in 30% and diabetes in 15% of the population. Though in our study 78.6% had 2 or more than 2 risk factors, study by Prabhakaran D has shown 47% of the respondents to have at least 2 of these risk factors.

Another study by Mohan et al in 2008, has shown prevalence of major risk factors for cardiovascular disease as: diabetes 11.9%; hypertension 25.4%; dyslipidemia 40.2%; hypertriglyceridemia 28.3%; overweight (body mass index \geq 23 kg/m²) 60.2%; and metabolic syndrome 34.1%.

Various other studies have also shown similar trends in the Indian population. An increasing prevalence of impaired glucose tolerance and diabetes in urban residents of Chennai has been reported by Ramchandran et al. Smoking and low physical activity have been shown to be prevalent in 20-39 year old urban adults by Gupta et al in 2002. Another important independent risk factor for CAD is family H/O of CAD as reported by Goel et al in 2003.

Our study has clearly shown that prevalence of obesity, hypertension, dyslipidemia, diabetes are increasing among the middle class of the Indian population and these modifiable risk factors are responsible for the high prevalence of CAD risk factors. Study has shown direct correlation of increased BMI with dyslipidemia, diabetes and hypertension. CAD has a multi factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as consequence of urbanization may partly explain the escalation of CAD. India is experiencing an epidemiological transition with high rates of urbanization. This has led to economic improvement, the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. With the introduction of an era of refined foods, sugar and hydrogenated oils, the traditional high complex carbohydrate, high fibre and low fat diet has been replaced by a diet rich in fats and simple sugars low in dietary fibres. One of the effects of this transition is a shift in the disease spectrum from the communicable to non communicable diseases particularly CAD and Diabetes. More importantly the disease is affecting the young Indians i.e. the productive workforce. The incidence of CAD in young Indians is 12-16% which is higher than any other ethnic group. Lack of awareness of the preventable risk factors and ignorance of the disease is also an important factor responsible for the increasing rate of CAD among Indians. In the present study out of 21% hypertensive study subject only 4.76% were aware of the condition and were on

MANUSCRIPT

medication and 16.22% were identified during the study. Similarly, out of 16% diabetics, 5.6% were fresh diagnosed. This shows that awareness and control of hypertension and diabetes was poor in the study population, indicating low detection and poor management of major CAD risk factors.

Prevention and control of the risk factors of CAD can reduce the rate of CAD. It needs changes in the individual as well as changes at the community level. Taking care of modifiable factors such as smoking, increases levels of body fat, too much use of fat and salt in food, sedentary lifestyle together with the use of accessible and affordable preventive medicines can definitely make a difference as far as CAD is concerned. Help of the television and media can be utilized to create awareness among the masses. Local Resident Welfare Associations and religious groups can also be empowered to promote healthy lifestyle and exercise among the community.

CONCLUSION

The present study demonstrates high prevalence of CAD risk factors in the Indian population as study population was representative of the national population and it does represent the rising trend of CAD in urban India. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors, promotion of right diet and physical activity and at the same time development of the guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

MANUSCRIPT

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CONTRIBUTORSHIP STATEMENT

Sekhri T1* Principal investigator of the study, Kanwar RS1 Co principal investigator of the study and also involved in medical evaluation and manuscript writing, Wilfred R1 medical evaluation of the study subjects and data compilation, Chugh P1 medical evaluation of the study subjects and data compilation,, Chhillar M1 medical evaluation of the study subjects and data compilation,, Aggarwal R1 medical evaluation of the study subjects and data compilation,, Sharma YK2 statistical evaluation and analysis of study population, Sethi J1 dietary evaluation and data compilation, Sundriyal J1 laboratory sample analysis, Bhadra K1 laboratory sample analysis, Singh S1 laboratory sample analysis laboratory sample analysis Rautela N1 laboratory sample analysis, Tekchand1 laboratory sample analysis, Singh M1 laboratory sample analysis, Singh SK1 laboratory sample analysis.

COMPETING INTERESTS

None

DATA SHARING STATEMENT

No additional data

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MANUSCRIPT

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MANUSCRIPT

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(Sanction letter No. DLS/81/48200/INM-310/1060/D(R&D) dated 16 May,2007)

**STUDY OF THE HEALTH PROFILE OF DRDO
EMPLOYEES WITH SPECIAL EMPHASIS ON
CORONARY RISK FACTORS**



**R&D PROJECT
(2006-2010)**

INSTITUTE OF NUCLEAR MEDICINE & ALLIED SCIENCES

*Brig. SK Mazumdar Road,
Delhi-110054*

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Objectives: -

1. To carry out cross sectional survey of DRDO population and study the prevalence of conventional coronary risk factors in DRDO employees.
2. To identify the high risk population for CAD
3. To prepare psycho-social profile of the subset of study population (Delhi population)
4. To determine a vulnerability index based on the profile
5. To suggest the measures for dietary interventions and primary prevention
6. To study the newer emerging coronary risk factors in the subset of study population
7. To study the gene expression profiles in CAD patients and controls (30 subjects in each group).
8. To study the association of SNPs in CAD using custom designed arrays in 500 samples.
9. To determine the antibody titres of various hsps such as hsp60, hsp70,hsp90 etc in subset of 100 subjects in each group

Scope:-

Coronary artery disease is a common cause for morbidity and mortality. Earlier mainly confined to developed countries and the incidence were significantly less in the poor and developing countries. But now the disease is widespread and the Indians are more prone to this disease as compared to the other developing countries and with almost same economic status (1).

In the coronary artery disease in Asian Indian (CADI) study, the prevalence of CAD was 10.2% (2) compared with 2.5% (3) in white men of the same age group in the Framingham offspring study. The high rates of CAD among Asian Indians are in sharp contrast to the low rates of CAD among other Asian. Despite very high rates of smoking and hypertension, the CAD rates in Japan are 4 fold lower than in the US (Japanese paradox) (4). The same is true in China (Chinese paradox) (5).The CAD rates in rural India are one half that of urban India, though smoking is more common in Indian villages. However, these rural rates are double that of the overall US rates and 4 fold higher than in rural China and Japan.

The Framingham heart study, since 1948, in Framingham town of USA, has been the landmark epidemiological study that examined longitudinally the development of CAD in a general adult population. It pioneered the concept that certain attributes or exposures known eventually as the risk factors were associated with the development of heart disease. The

Original Research Protocol

concept of risk factors spawned a new generation of studies aimed at interventions to reduce the impact of risk factors on health.

Risk factor concept is now firmly established by Kannel & McGee (1987). CAD is best conceptualized as a multifactorial disease process, with no individual risk factor strictly essential or sufficient for causation.

There are many known risk factors causing the CAD which are accepted worldwide. These risk factors are divided into conventional risk factors like hypertension, Diabetes mellitus, hyperlipidemia, smoking, obesity, sedentary life style, mental stress, family history of CAD. Recently there have been focus on the other factors which are considered to be the important in genesis of the coronary artery disease; these are called newer coronary risk factors. The studies have shown they are as important as the conventional risk factors (6).

Risk factors have been categorized by several properties as follows (7):

Category I: Risk factors for which interventions have been proved to reduce the incidence of CAD events.

- 1. Cigarette smoking
- 2. Low density lipoproteins cholesterol
- 3. Hypertension
- 4. Left ventricular hypotrophy
- 5. Thrombogenic factors viz antiphospholipid antibody in SLE, homocysteine in homozygous homocystinuria, plasminogen activator inhibitor-I antigen etc.

Category II: Risk factors for which interventions are likely to lower CAD events.

- 1. Diabetes mellitus
- 2. Physical inactivity
- 3. HDL cholesterol
- 4. Postmenopausal status - case-control and cohort studies suggest that estrogen replacement results in 50% reduction in the risk of developing CAD(8,9)

Category III: Risk factors clearly associated with an increase in CAD risk, which, if modified, might lower the incidence of CAD events.

Original Research Protocol

1. Psychosocial factors
2. Triglycerides
3. Lipoprotein(a)
4. Homocysteine
5. Oxidative stress
6. Alcoholic beverage consumption

Category IV: Risk factors associated with increased risk but which cannot be modified or whose modification would be unlikely to change the incidence of CAD events.

1. Age
2. Gender
3. Family history
4. Genetic factors

Autopsy studies (10-13) show that coronary atherosclerosis begins as early as 20 years of age, and a recent study found severely stenotic coronary arteries (Narrowing \geq 40%) in 19% of men in their early thirties (14). On the basis of these observations, the National Cholesterol Education Program recommended cholesterol screening in all adults 20 years of age or older (15). Similarly, the sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends screening for hypertension in all persons 18 year of age or older (16). However, guidelines on prevention of coronary heart disease in young adults have not been uniformly accepted, in part because data on risk prediction and coronary disease prevention in adults younger than 40 years of age are limited (17-20).

In Indian studies Reddy et al (21) documented the high prevalence of smoking, elevated serum cholesterol levels, low HDL levels, hypertension and diabetes in both the urban and rural population sampled. Similarly in the urban population studied in Chennai(22), serum levels of total cholesterol, LDL, TG were linked to the presence of CAD. This study also documented the predisposition of people with diabetes and impaired glucose tolerance(IGT) to develop CAD. The prevalence of CAD was 21.4% in diabetics and 14.9% in IGT and 9.1% in non diabetics. Numerous studies in middle-aged (40 to 65 years of age) and, to a lesser extent, older persons have shown that the major risk factors for coronary heart disease (which include cholesterol level, blood pressure, and cigarette smoking) are predictive of long-term outcomes in these age groups (23-26).

In addition, primary and secondary prevention trails have convincingly shown benefits of reduction of certain risk factors, such as dyslipidemia and hypertension, in middle-aged and older adults (15, 16, 27-29). However, equally compelling data from observational studies or clinical trials are almost nonexistent in young adults (12, 13, 23, 30). Manchanda et al demonstrated regression of coronary atherosclerosis in patients with severe coronary artery disease by yoga lifestyle intervention(31).

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Very recent study compared primary prevention and secondary prevention and concluded that primary prevention achieved a fourfold larger reduction in deaths as compared to secondary prevention (32)

Psychosocial factors in CAD

The link between the body and mind is a very powerful one. Most of the disease have been linked not only with the condition of the body but with the state of mind as well. Coronary artery disease (CAD) is no exception. CAD is prevalent in near epidemic proportions in the Indian subcontinent (Banerjee, 2001)(33) and Myocardial Infarction (MI) is a major cause of death in the4 world. Research has linked several risk factors to cardiovascular disease. A risk factor is any characteristic or condition that occurs with greater frequency in people with a disease than in people who are free from that disease. It neither helps in identification of a cause nor a prediction of who will not be affected. It yields information concerning which conditions are associated directly or indirectly with a particular disease or disorder. The Framingham heart study (1948, 1971) uncovered a number of risk factors.; These include inherent risk, physiological risk, behavioural and life-style risks, and psychosocial risks, Inherent risk factors cannot be changed, such as family history, age, gender and ethnicity. Physiological risk factors include hypertension and high cholesterol. Behavioural risk factors include smoking and a diet high in saturated fat and low in fiber and antioxidant vitamins. Psychosocial factors include persistently high levels of anxiety, stress, low educational level, low income, lack of social support and both expressed as well as unexpressed anger. Despite a number of researches being conducted in this field, we know only about half the risk factors for heart disease (Voelker, 1998) (34).

Chronic anger, anxiety, loneliness and depression have been reported as major emotions by Garnett, 1996(35). Similar studies have found that suffering from anxiety and having feelings of anger and hostility also increase one's risk of dying from CAD. Harvard researchers found that patients who reported two or more anxiety symptoms at the beginning of the study had four times the risk of dying from a heart attack. A prospective study (Kavachi et al., 1994)(36) showed that men who experienced phobic anxiety were three times more likely to suffer sudden death from heart disease than their counterparts.

Garnett (1996)(35) found that the risk of heart attack was 2.3 times greater than expected if the person had been angry two hours before the event. Constant, unrelieved stress overtaxes the heart and raises the blood pressure, cholesterol and fat levels in the blood (Ornish, 1990)(37), increasing the likelihood of CAD. Psychosocial factors such as low socio-economic status and low educational level are two additional factors for heart disease (Eaker, Pinsky and Castelli, 1992, Gillum et al., 1998, Fried, 1998)(38-40).

Original Research Protocol

Being single and lacking social support are also coronary risk factors (Williams, 1992, Case et al., 1992)(41,42).

A large body of research supports the view that hostility is a better predictor of CAD than Type A behaviour (Williams et al, 1980) (43). The expression of anger hostility is positively related to CAD (Siegman, Dembroski & Ringel, 1987). Dembroski et al., (1985)(44,45) found a significant association between anger in scores and CAD. A study by Appels et. al., postulated that prolonged and uncontrollable psychological stress (either at work or family situations) may result in a state called "vital exhaustion" (lack of energy, increased irritability and demoralization) that need to be addressed (Kop, 1997)(46). Individuals with high job demand but low job latitude are under job strain, performing excessive routine work with lack of creative outlets (Karasek et al., 1981)(47) or with effort reward imbalance (Peter et al., 2002)(48), are susceptible to CAD.

Thus, the impact of psychosocial factors in CAD cannot be ignored. It therefore becomes imperative that a thorough screening of these psychosocial factors (as mentioned above) is carried out in addition to the various routine tests of CAD. This is essential for determining the susceptibility of an individual to be affected by heart disease and for the development of effective therapeutic intervention and follow-up.

Genetic susceptibility in CAD

Coronary artery disease (CAD) is a chronic inflammatory disease, progression of which may be accelerated by immunological mechanisms. Genes involved in regulation of inflammation and protection against infectious agents may affect severity of the disease. Major Histocompatibility Complex (MHC) region carries genes involved in innate and adaptive immunity and inflammation. These genes contain components of the complement (C2, factor B, C4A and C4B), cytokine genes (tumor necrosis factor and lymphotoxin-alpha (LTA), stress response genes (heat shock proteins) and the HLA class I (HLA-A, HLA-B, HLA-C) and class II (HLA-DRB, HLA-DQB, HLA-DPB) genes for the initiation of specific immune responses.

It was reported that the relative risk for coronary artery disease is increased if a person had human leukocyte antigen BW 38 (Stone et al., 1981)(49). This study showed a statistically significant trend between the presence of HLA BW 38 and premature CAD. In another study it has been reported whether donor or recipient HLA type influenced the development of CAD in cardiac allograft recipients. They found that the particular MHC class II types in the donor heart predispose to accelerated CAD, perhaps by inducing a more vigorous immune response in the recipient. However, it is becoming apparent that MHC

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genes alone can not account for the genetic susceptibility to the diseases with which they are associated. Most of these disorders appear to be complex genetic traits where the MHC is only one of several (or many) interacting genes, which along with environmental stimuli, ultimately lead to a pathological condition. Thus if there is genetic susceptibility to CAD, HLA is likely to be only part of the genetic equation. If subsequent investigations confirm a link between susceptibility to CAD and MHC alleles, a new dimension will be opened in the exploration for mechanisms underlying this seemingly nonimmunologic disease as well as potentially other forms of the disease.

Large-scale quantitative analysis of gene expression, including cDNA microarrays and proteomic analysis, is now applied to heart failure and atherosclerosis. The technology is still at the beginning and is limited by variations in the array platforms and gene products as well as sensitivity or specificity of the selected probes. But, this method has the advantage of: (1) simultaneous screening of hundreds of genes and identification of the up/down-regulated genes in a particular condition or tissue, (2) identification of pathways and monitoring of expression of underlying genes responsible for a disease, and (3) identification of possible target molecules/ genes for future therapeutic studies. With these advantages the microarray analysis for gene expression is a preferred high-throughput tool for candidate gene(s) identification.

The precise molecular mechanisms that lead to coronary artery disease (CAD) are not understood, despite a wealth of knowledge on predisposing risk factors and pathomechanisms. The biological complexity of CAD results from unknown or unpredictable interactions of many genetic and environmental factors which, by themselves, have only been partially identified. According to current knowledge, genetic variations in causative or susceptibility genes form the basis of molecular mechanisms that, together with environmental impact, lead to CAD and determine its clinical course. Studies at molecular level have identified gene clusters/ families like apoE-CI-CII (Wang et al. 2006)(50), interleukins specially IL-18 and sICAM-1 (Mironczuk et al. 2005)(51), MEF2A (Kojimoto et al. 2005)(52), monocyte adhesion and diapedesis, lipid metabolism and fibrinolysis regulation responsible genes like ICAM1, APOE, PPARA and PAI-1 (Zak et al. 2005)(53), gene for collagen receptor alpha2beta1 (Ajzenberg et al. 2005)(54), TNFα (Bernard et al. 2003, Csiszar et al. 2006, Giacconi et al. 2006)(55-57), nitric oxide synthase (eNOS) gene polymorphisms (Yoshimura et al. 2000, Rossi et al. 2006, Morawietz et al. 2006)(58-60), Calcium dependant enzymes like paraoxonase (PON1; Laplaud et al. 1998)(61), hsCRP (Rasouli and Kiasali 2006)(62), metalloproteinases (MMPs, Fitzsimmons et al. 2006)(63), urotensin II (U-II, Watanabe et al. 2006)(64), Monocyte chemoattractant protein-1 (MCP-1, Kim et al. 2006)(65), GATA2 (Connelly et al. 2006)(66), Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (Fan et al. 2006)(67), insulin-like growth factor-I receptors (IGF-IR) and insulin receptors (IR) (Chisalita et al. 2006)(68) and heterotrimeric G-proteins (Renner et al. 2006)(69) and related genetic polymorphisms lead to CAD. But lack of precise clinical phenotyping, lack of functional characterization of gene variants, and the vast number of yet undetected genes may provide some explanation of CAD progression. Except for certain polymorphisms in lipid genes (i.e. apolipoprotein E [apo E]) or rare genetic variations (i.e. LDL receptor), which have a causal effect on both the intermediate (LDL-

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cholesterol level in plasma) and the clinical phenotypes (CAD), the role of most gene polymorphisms is controversial or unknown. Despite the enormous progress in sequencing the human genome and in molecular genetic and bioinformatic techniques during the past decade, the progress in identifying genes responsible for complex traits such as CAD has been modest and presents a formidable challenge to medical research constraining drug development programmes. No such information is available for Indian population and no SNP polymorphism has been associated with CAD for Indian populations.

The 70 kilodalton heat shock proteins (Hsp70s) are a family of ubiquitously expressed [proteins](#). These proteins are an important part of the cell's machinery for protein folding, and help to protect cells from stress. Apart from chaperoning tumor-specific peptides, HSPs per se provide activatory signals for the innate immune system. Hsps are also reported to be pro-atherogenic by stimulating proinflammatory cytokine production in atherosclerotic lesions contributing to plaque rupture (Giacconi et al. 2006)(57). In fact, the 1267 HSP70-2 polymorphism has been reported to be independently associated with coronary artery disease (CAD). More over this 1267 HSP70-2 polymorphism has also been established as a risk factor for carotid plaque rupture and cerebral ischaemia in old type 2 diabetes-atherosclerotic patients (Giacconi et al. 2005)(70). But patients with coronary atherosclerosis reported to possess lower levels of anti-HSP70 antibody levels (Herz et al. 2006)(71). Wu et al., (1999) found increased anti-hsp60 titres were associated with hypertension and atherosclerosis.

This project will study the prevalence of conventional and newer emerging coronary risk factors in DRDO staff. We will also find the prevalence of CAD in DRDO staff and emphasize preventive measures.

INSTITUTIONAL ETHICS COMMITTEE FOR HUMAN TRIALS (IEC)
INSTITUTE OF NUCLEAR MEDICINE & ALLIED SCIENCES (INMAS)
DRDO, Ministry of Defence, Brig S K Mazumdar Marg, Delhi – 110 054
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INM/TS/IEC /002/07
Date: 27/09/2007

Chairman **Member Secretary**
Prof. Y K Gupta Dr. Tarun Sekhri

Members

Prof. Anju Seth, Mr. A S Aggarwal, Dr. A K Mishra, Dr. A Salhan,
Dr. N K Chaudhary, Dr. G Sripathy, Dr. S C Jain

To

Dr Tarun Sekhri, Sci 'F'
INMAS,
Brig S K Mazumdar Marg
Delhi – 110 054

Subject: Ethical clearance of your submitted project by the IEC.

The IEC considered the following project submitted by you:

"Study of the health profile of DRDO employees with special emphasis on coronary risk factors"

The IEC gives approval for the study.

(Dr. Tarun Sekhri)
Member Secretary

Copy to:

1. Director, INMAS – for information
2. Head, Tech coord

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract [YES] Addressed in manuscript page no 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found [YES] Addressed in manuscript page no 1
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported [YES] Addressed in manuscript page no 2
Objectives	3	State specific objectives, including any prespecified hypotheses [YES] Addressed in manuscript page no 2
Methods		
Study design	4	Present key elements of study design early in the paper [YES] Addressed in manuscript page no 3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [YES] Addressed in manuscript page no 3
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants [YES] Addressed in page no 3 & 4 (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [YES] Addressed in manuscript page no 3 & 4
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [YES] Addressed in manuscript page no 3&4
Bias	9	Describe any efforts to address potential sources of bias [NOT APPLICABLE]
Study size	10	Explain how the study size was arrived at [YES] The employees working in National level organisation were requested to participate in the study. Those people who agreed voluntarily were made a part of study. Out of a total 40000 employees, 14500 agreed to take part in the study. Manuscript Page no 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [YES] The risk factors of CAD were independently studied. Each variable was studied as per the normal range for common clinical parameters.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding [YES] Addressed in manuscript page no 6 (b) Describe any methods used to examine subgroups and interactions [YES]

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Addressed in manuscript page no 6

(c) Explain how missing data were addressed **[YES] The subjects whose data could not be completed for some reason or other were excluded from the study.**

(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed
Case-control study—If applicable, explain how matching of cases and controls was addressed **[NOT APPLICABLE]**
Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy **[YES] Addressed in manuscript page no 6**

(e) Describe any sensitivity analyses

Continued on next page

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Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [YES] Addressed in manuscript page no 6 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [YES] Addressed in manuscript page no 6 (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures [YES] Addressed in manuscript page no 6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [NOT APPLICABLE] (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [NOT APPLICABLE]

Discussion

Key results	18	Summarise key results with reference to study objectives [YES] Addressed in manuscript page no 8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [NIL]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [YES] Addressed in manuscript page no 8 & 9
Generalisability	21	Discuss the generalisability (external validity) of the study results [YES] Addressed in manuscript page no 8 & 9

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [YES] Addressed in manuscript page no 9
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Prevalence of risk factors for coronary artery disease in urban Indian population

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	CARDIOLOGY, Cardiac Epidemiology < CARDIOLOGY, Coronary heart disease < CARDIOLOGY



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MANUSCRIPT

Prevalence of risk factors for coronary artery disease in urban Indian population

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MANUSCRIPT

ABSTRACT

Objective: The objective of the study was to assess the prevalence of risk factors for coronary artery disease in government employees workers posted across the country.

Methods: The study population included subjects from ministry of government employees posted in different parts of the country {Males (n=10642), Females (n=1966) aged 20 to 60 years} and comprised of various ethnic groups, staying in different environmental conditions. The recruitment was done across India in 14 states, 20 cities, and, one union territory. All the following individuals were subjected to detailed questionnaire, medical examinations and anthropometric measurements. Blood samples were collected for blood glucose and serum lipid profile estimation. Resting ECG was also recorded for these subjects. Results were analyzed by using appropriate statistical tools.

Results: The study revealed that the family history of premature CAD was present in 4.6% of the study population. The overall prevalence of Diabetes was 16% and out of 16% diabetics, 5.6% were freshly diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication. Hypertension was present in 21% of subjects. Prevalence of dyslipidemia was significantly high with 45.6% of study subjects having high total cholesterol/HDL ratio. 78.6% Subjects had 2 or more risk factors for CAD.

Conclusion: The present study demonstrates high prevalence of CAD risk factors in the Indian urban population. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors to manage individuals at high risk for future CAD.

STRENGTHS & LIMITATIONS OF THE STUDY

- Our study is the first of its type where population was covered across various cities in India. The study population included people of various ethnicities, age groups, and living in different parts of the country.
- There are very few studies across the world where such a large population were studied for the conventional risk factors of CAD.
- The history and clinical examination of the subjects were collected by qualified doctors who interviewed & examined each subject of the study. All the biochemical investigations were performed by the same team using similar kits and evaluation technique.
- The limitation of the study was that out of approximately 26000 working population of this organisation only 14500 gave informed consent to participate in the study. Out of these subjects data could be completed in 12608 subjects and was statistically analysed.
- Because of the limited resources in Phase I we could study and evaluate only the conventional coronary risk factors.

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INTRODUCTION

Coronary Artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries. It is a leading cause of death in India, and its contribution to mortality is rising; deaths due to CAD are expected to double from 1985 to 2015.[1] According to the reports of National Commission on Macroeconomics & Health, there would be 62 million patients with CAD in 2015 in India and of these 23 million would be patients younger than 40 years of age.[2]The prevalence of classical cardiovascular (CV) risk factors (CVRFs) such as hypertension, dyslipidemia, obesity and diabetes varies widely between different countries, and shows some important secular trends. The conventional risk factors of CAD can be divided in non-modifiable and modifiable risk factors. The former include age, sex and family history while the latter include diabetes mellitus, smoking, dyslipidemia, hypertension and obesity. There is increasing incidence to believe that Asian Indians are at an increased risk of CAD, which cannot be attributed to the common risk factors. Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of the CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrated that Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI-1) and homocysteine levels.[3] The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes i.e. changes in diet, physical inactivity, drug and alcohol intake etc, and increase in prevalence of diabetes mellitus.[4,5] The prevalence of risk factors in a population determines the future burden on health care services and loss of productive years of a particular person. It is not only a health risk for that individual but overall burden on the economy. There are no large scale studies of adequate sample size to evaluate the prevalence rate, risk factor patterns and electrocardiographic changes in Indian populations. This study was planned to evaluate the future risk of CAD in a national level organization. The organization has offices across the entire country (Fig 1). So the study population included subjects from various ethnic groups, staying in varied environments and consuming different varieties of diet. To the best of our knowledge our study is the first such study carried out across India, where the employees are working all over India and belong to different ethnicity spread across the country.

Key words

CAD: coronary artery disease; **BP:** blood pressure; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure; **FPG:** fasting plasma glucose; **PPPG:** post-prandial plasma glucose; **BMI:** body mass index; **LDL-cholesterol:** low-density cholesterol; **HDL-cholesterol:** high density cholesterol; **CVRFs:** cardiovascular risk factors

MATERIAL AND METHODS

Patient Population and Study Design

All the subjects were civilian government employees posted in various parts of the country. The subjects of both the sexes were recruited after written informed consent. They fall in the age groups ranging from 20 to 60 years. The recruitment was done across India in 14 states, 20 cities, and, one union territory namely, Delhi (Delhi), Karnataka(Bangalore, Mysore), Andhra Pradesh (Hyderabad, Vishakahapatnam), Maharashtra (Pune, Ambernath, Ahmednagar), Uttar Pradesh (Agra, Kanpur), Rajasthan (Jodhpur), Himachal Pradesh (Manali), Chandigarh, Uttrakhand (Dehradun, Mussourrie), Orissa (Chandipur), Assam (Tejpur), Jammu & Kashmir (Leh), Madhya Pradesh (Gwalior), Tamil Nadu(Chennai), Kerala (Kochi). This data collection involved subjects from different states of India like Delhi, Maharashtra, Karnataka, Tamil Nadu, Kerala, UP, Uttrakhand, Himachal Pradesh, Rajasthan, Orissa etc. This is an ongoing study and now is in its phase 2. The patient recruitment was initiated in 2009 and the phase 1 evaluation was completed in 2012.Of the initial 14,000 subjects sampled, 1500 subjects were considered as non-eligible and a sample of 12,500 was subjected to detailed statistical analysis and evaluation. The sample size calculation was not performed as it was an open study where voluntary participation of all employees was encouraged.

Ethical Clearance

The study was approved by the Institutional Ethics Committee of Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi.

Inclusion criteria

- a. Civilian government employees posted in various parts of the country
- b. Apparently healthy individual
- c. Age 20 – 60 years
- d. Both the sexes

Exclusion criterion

- a. Known case of coronary artery disease (CAD)

Assessment process

Participants were asked to attend the Health Center of their respective institution at 8:00 am after an overnight fast. They were asked to continue their medication if any, as usual. A detailed questionnaire was applied by medical personnel prior to clinical measurements and blood collection. The questionnaire recorded information on demographic data, socio-economic and marital status, and several lifestyle factors namely tobacco, alcohol and caffeine consumption, physical activity, family history, disease history, medication use, and family history of premature CAD in first degree relatives (age <55 years in men & <65 years in women).In women, further data regarding reproductive and obstetrical history, oral contraception and hormonal replacement therapy was collected.

Anthropometry and clinical examination including blood pressure measurement was carried out. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5mm using a height gauge. Body mass index (BMI) was defined as weight in Kg/ (height in meters) ².

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Blood pressure (BP) and heart rate were measured on the left arm, with an appropriately sized cuff, after at least 10 minutes rest in the seated position using an automated BP instrument. The average of the last two measurements was used for analysis. The subjects diagnosed to have high BP for the first time were called again the next day for BP monitoring before labeling them as hypertensive. In addition, waist and hip circumferences were measured as recommended. Resting ECG was also obtained as a part of evaluation.

Blood samples were collected in the fasting state and 2 hours after 75 grams of oral glucose. Biochemical evaluation of the blood samples included complete blood count, Fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), lipid profile, and liver & kidney function tests. The clinical chemistry tests were performed on fresh blood samples using automatic analyser on the same day. Subjects whose FPG was ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl were diagnosed as fresh cases of Diabetes Mellitus. Other subjects with past history of DM and/or taking medication for the same were also considered as Diabetics.

In the evaluation of Lipid profile the value of Total cholesterol/HDL cholesterol ≥ 4.5 was considered abnormal. Known cases of dyslipidemia and/or those on medication for the same were also included in dyslipidemia risk factor.

Table no. 1. Definitions for different risk factors in the study

Risk factor	Definition
Hypertension	Systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) ≥ 90 mm Hg during the visit and/or presence of anti-hypertensive drug treatment and was considered as known if the subject was aware of this condition.
Diabetes Mellitus	FPG ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl at the time of investigations and/or presence of anti-diabetic drug treatment and was considered as known if the subject was aware of this condition.
Obesity	BMI ≥ 30 kg/m ²
Overweight	BMI ≥ 25 kg/m ² .
Hypercholesterolemia	Total blood cholesterol ≥ 200 mg/dl
Decreased High density lipoprotein(HDL) cholesterol	≤ 40 mg/dl
Adverse total cholesterol/High density lipoprotein ratio (Dyslipidemia)	≥ 4.5
Age	>45 years in men; >55 years in women
Sex	Male sex
Family History of CAD	Premature CAD in first degree relatives (<55 years in men & <65 years in women)
Risk factors for CAD	age, sex, family history, diabetes mellitus, smoking, dyslipidemia, hypertension and obesity

The strength of the study is that each participant had one on one interaction with at least one of the project team doctors. Each questionnaire was scrutinised by the doctor. So this added value to the data. In most of the epidemiological studies usually paramedics collect the data.

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Statistical Analysis

The final data was recorded on a predesigned Performa and managed in Microsoft access. The data analysis was performed using SPSS 20.0. The values of various parameters are presented as mean and SD (standard Deviation), in absolute numbers and as percentage. Comparison between male and female was done by t-test. Correlation statistics between various risk factors was also computed. Minimum Significance level was set at 0.05.

RESULTS

A total of 14,500 subjects were evaluated in the study. After informed consent, exclusion criteria, clinical & biochemical assessment, complete data of 12,608 cases (Males – 10,642 Females – 1,966) was available for final analysis. Mean age of males was 44.34±10.63 & median age being 47.00 years. Mean age of females was 42.47±10.34 and median age was 44.00 years. Baseline characteristics are shown in Table no. 2 .

Table no.2: Baseline characteristics of the study population (n=12,608)

Parameters ± SD	MALES (n=10642)	FEMALES (n=1966)	P value
Age	44.34±10.63	42.47±10.34	.000
Height	166.92±6.89	154.74±6.34	.000
Weight	69.36±10.69	62.24±11.30	.001
BMI	24.89±3.58	26.02±4.69	.001
Systolic BP	127.35±16.12	120.05±15.25	.000
Diastolic BP	81.08±10.04	77.05±9.60	.000
FPG	95.91±31.08	93.48±32.10	0.01
PPPG	135.44±56.31	131.86±54.47	.01
Total Cholesterol	186.11±40.56	181.69±36.62	.001
HDL	42.46±11.55	46.54±11.36	.001

Different parameters considered for calculating the risk factors and their results are depicted in Table no. 3.

Table no.3: Percentage (%) of Risk factors in study population (n=12608)

Parameters	Total (n=12608)	MALES (n=10642)	FEMALES (n=1966)	P value
Family H/O CAD	580(4.6%)	460(4.4%)	120(6%)	<.05
Smoking	1471(11.6%)	1469(13.8%)	2(0.1%)	<.001
BMI >25 kg/m ²	6002(47.6%)	4910(46.1%)	1092(55.5%)	
Mean(SD)		27.8 ±3.59	29.17± (3.66)	<.001

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BMI 25-30 kg/m²	4959(39.3%)	4200(39.46%)	759(38.6%)	
Mean(SD)		26.93± 1.31	27.35± 1.44	<.001
BMI ≥30 kg/m²	1029(8.2%)	700(6.6%)	329(16.7%)	
Mean(SD)		32.78 ± 4.00	33.41± 3.74	<.05
Diabetes Mellitus	2016 (16%)	1766(16.6%)	250 (12.7%)	Ns
Hypertension	2647 (21%)	2383(22.4%)	264(13.4%)	<.001
Dyslipidemia	5755 (45.6%)	5137 (48.27%)	618 (31.4%)	<.001

Family history of premature CAD was present in 4.6% of the study population. The history of CAD in first degree relatives in males was 4.4% and in females was 6% (P value<0.05).

The prevalence of smoking was significantly higher in the men (13.8%) than females (0.1%), p value<0.001.

Out of 12603 study subjects, 6002 (47.6%) had BMI ≥25kg/m² with 4910(46.1%) males and 1092(55.5%) of females, P value<0.001. On further analysis it was observed that 39.46% males and 38.6% of females were overweight with BMI 25-30 kg/m², P value<0.001. The mean BMI of the overweight males was 26.93±1.31 and 27.35±1.44 of females. Obesity with BMI ≥30 kg/m² was present in 6.6% of males with mean BMI of 32.78 ±4 and 16.7% of females with mean BMI of 33.41 ±3.74, p value <0.05.

Overall prevalence of Diabetes was 16% in study population with no significant difference present in male (16.6%) and female (12.7%) subjects. Out of 16% diabetics, 5.6% were fresh diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication.

Out of 10642 male subjects, 2383 (22.4%) were found to have hypertension, whereas out of 1966 female subjects, 264 (13.4%) had high BP, p value<0.001. Overall prevalence of hypertension was 21% in the study subjects. Of these subjects only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study.

The prevalence of dyslipidemia in study population was significantly high with 45.6% of study subjects having high total cholesterol/HDL cholesterol ratio. 48.27% of male subjects and 31.4% females were found to have dyslipidemia (P value<0.001). The prevalence of hypercholesterolemia in study population was 31.3% with no significant difference in men (32%) and women (27.6%). When the cut off value of low HDL was used as 40 mg/dl for men its prevalence was found to be 37.7% and similarly at a cut off value of low HDL less than 50 mg/dl for women its prevalence was 76%.

Total number of subjects having 2 or more than 2 risk factors for CAD was 9909 (78.6%). 9251 (86.9%) male subjects had 2 or more than 2 risk factors in comparison to 658 (33.46%) females. The most prevalent risk factor in men was dyslipidemia present in 48.27% of males followed by BMI>25 present in 46.1% of males. Whereas in women BMI>25 was most prevalent factor present in 55.5% of women, followed by dyslipidemia in 31.45%.

HDL correlated negatively with FPG, PPPG, and BMI. BMI had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose and total cholesterol. Total cholesterol had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose, BMI (Table No. 4).

Table No 4. Correlations by Pearson correlation (2 tailed); (n=12608)

Parameters	BP Systolic	BP Diastolic	FPG	PPPG	Serum Total Cholesterol	Serum HDL	BMI
BP systolic	1	.715(**)	.149(**)	.136(**)	.086(**)	-.011	.190(**)

MANUSCRIPT

BP Diastolic	.715(**)	1	.119(**)	.107(**)	.114(**)	-.011	.216(**)
FPG	.149(**)	.119(**)	1	.821(**)	.095(**)	-.054(**)	.099(**)
PPPG	.136(**)	.107(**)	.821(**)	1	.092(**)	-.042(**)	.117(**)
Serum Total Cholesterol	.086(**)	.114(**)	.095(**)	.092(**)	1	.000	.063(**)
Serum HDL Cholesterol	-.011	-.011	-.054(**)	-.042(**)	.000	1	-.068(**)
BMI	.190(**)	.216(**)	.099(**)	.117(**)	.063(**)	-.068(**)	1

** Correlation is significant at the 0.01 level (2-tailed).

Discussion

The present study deals with finding the prevalence of the risk factors of the CAD, in a national level organization where people from different regions of India work. The employees were of both the sex and age group of 20-60. In the present population of the study, we found that approximately half of the population had dyslipidemia (45.6%) and BMI above 25kg/m² (47.6%). About one fifth of the study population was hypertensive (21%) and one sixth had Diabetes mellitus(16%). 78.6% of the study population had 2 or more than 2 CAD risk factors which indicates that there is a large population who in the near future will develop CAD.

The results of our study can be compared with the results of Jaipur Heart Watch-5 done by Rajeev Gupta et al on 739 subjects with 451 men and 288 women. In the study, overweight/obesity was present in 46.2% in males and 50.7% of females. [6]Prevalence of Hypertension was 39.5% in males and 24.6% of females. Diabetes was present in 15.5% of males and 10.85 of females. 33% of the males and 32.7% of the females had high cholesterol levels.

Similar results are shown by a study done by Prabhakaran D et al among men working in an industry of Northern India.[7] It showed high serum total cholesterol/HDL ratio in 62%, overweight in 47%, hypertension in 30% and diabetes in 15% of the population. Though in our study 78.6% had 2 or more than 2 risk factors, study by Prabhakaran D has shown 47% of the respondents to have at least 2 of these risk factors.

Another study by Mohan et al in 2008,has shown prevalence of major risk factors for cardiovascular disease as: diabetes 11.9%; hypertension 25.4%; dyslipidemia 40.2%; hypertriglyceridemia 28.3%; overweight (body mass index > or = 23 kg/m2) 60.2%; and metabolic syndrome 34.1%.[8]

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Various other studies have also shown similar trends in the Indian population.[9-15] An increasing prevalence of impaired glucose tolerance and diabetes in urban residents of Chennai has been reported by Ramchandran et al.[16] Smoking and low physical activity have been shown to be prevalent in 20-39 year old urban adults by Gupta et al in 2002.[17] Another important independent risk factor for CAD is family H/O of CAD as reported by Goel et al in 2003.[18]

Our study has clearly shown that prevalence of obesity, hypertension, dyslipidemia, diabetes are increasing among the middle class of the Indian population and these modifiable risk factors are responsible for the high prevalence of CAD risk factors. Study has shown direct correlation of increased BMI with dyslipidemia, diabetes and hypertension. CAD has a multi factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as consequence of urbanization may partly explain the escalation of CAD. India is experiencing an epidemiological transition with high rates of urbanization.[19-22] This has led to economic improvement, the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. With the introduction of an era of refined foods, sugar and hydrogenated oils, the traditional high complex carbohydrate, high fibre and low fat diet has been replaced by a diet rich in fats and simple sugars low in dietary fibres.[23] One of the effects of this transition is a shift in the disease spectrum from the communicable to non communicable diseases particularly CAD and Diabetes.[24-26] More importantly the disease is affecting the young Indians i.e. the productive workforce. The incidence of CAD in young Indians is 12-16% which is higher than any other ethnic group. Lack of awareness of the preventable risk factors and ignorance of the disease is also an important factor responsible for the increasing rate of CAD among Indians.[27-32] In the present study out of 21% hypertensive study subject only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study. Similarly, out of 16% diabetics, 5.6% were fresh diagnosed. This shows that awareness and control of hypertension and diabetes was poor in the study population, indicating low detection and poor management of major CAD risk factors.

Prevention and control of the risk factors of CAD can reduce the rate of CAD. It needs changes in the individual as well as changes at the community level. Taking care of modifiable factors such as smoking, increases levels of body fat, too much use of fat and salt in food, sedentary lifestyle together with the use of accessible and affordable preventive medicines can definitely make a difference as far as CAD is concerned. Help of the television and media can be utilized to create awareness among the masses. Local Resident Welfare Associations and religious groups can also be empowered to promote healthy lifestyle and exercise among the community.

CONCLUSION

The present study demonstrates high prevalence of CAD risk factors in the Indian population as study population was representative of the national population and it does represent the rising trend of CAD in urban India. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors, promotion of right diet and physical activity and at the same time development of the guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

MANUSCRIPT

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CONTRIBUTORSHIP STATEMENT

Sekhri T1* Principal investigator of the study, Kanwar RS1 Co principal investigator of the study and also involved in medical evaluation and manuscript writing, Wilfred R1 medical evaluation of the study subjects and data compilation, Chugh P1 medical evaluation of the study subjects and data compilation,, Chhillar M1 medical evaluation of the study subjects and data compilation,, Aggarwal R1 medical evaluation of the study subjects and data compilation,, Sharma YK2 statistical evaluation and analysis of study population, Sethi J1 dietary evaluation and data compilation, Sundriyal J1 laboratory sample analysis, Bhadra K1 laboratory sample analysis, Singh S1 laboratory sample analysis laboratory sample analysis Rautela N1 laboratory sample analysis, Tekchand1 laboratory sample analysis, Singh M1 laboratory sample analysis, Singh SK1 laboratory sample analysis.

COMPETING INTERESTS

There are no competing interests.

FUNDING

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DATA SHARING

Extra data of this project can be accessed by emailing Dr Tarun Sekhri, corresponding author at tarunsekhri@yahoo.com.

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Figure 1: The various labs in country where study was carried out

MANUSCRIPT

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Prevalence of risk factors for coronary artery disease in urban Indian population

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ABSTRACT

Objective: The objective of the study was to assess the prevalence of risk factors for coronary artery disease in ~~urban Indian population~~.

Methods: The study population included subjects from a ~~national level organisation situated~~ in different parts of the country {Males (n=10642), Females (n=1966) aged 20 to 60 years} and comprised of various ethnic groups, staying in different environmental conditions. The recruitment was done across India in 14 states, 20 cities, and, one union territory. All the following individuals were subjected to detailed questionnaire, medical examinations and anthropometric measurements. Blood samples were collected for blood glucose and serum lipid profile estimation. Resting ECG was also recorded for these subjects. Results were analyzed by using appropriate statistical tools.

Results: The study revealed that the family history of premature CAD was present in 4.6% of the study population. The overall prevalence of Diabetes was 16% and out of 16% diabetics, 5.6% were freshly diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication. Hypertension was present in 21% of subjects. Prevalence of dyslipidemia was significantly high with 45.6% of study subjects having high total cholesterol/HDL ratio. 78.6% Subjects had 2 or more risk factors for CAD.

Conclusion: The present study demonstrates high prevalence of CAD risk factors in the Indian urban population. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors to manage individuals at high risk for future CAD.

Comment [h1]:

Comment [h2R1]:

Comment [h3]: defence services workers posted across the country.

Comment [h4]: ministry of defence employees posted

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INTRODUCTION

Coronary Artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries. It is a leading cause of death in India, and its contribution to mortality is rising; deaths due to CAD are expected to double from 1985 to 2015.[1] According to the reports of National Commission on Macroeconomics & Health, there would be 62 million patients with CAD in 2015 in India and of these 23 million would be patients younger than 40 years of age.[2]The prevalence of classical cardiovascular (CV) risk factors (CVRFs) such as hypertension, dyslipidemia, obesity and diabetes varies widely between different countries, and shows some important secular trends.The conventional risk factors of CAD can be divided in non-modifiable and modifiable risk factors. The former include age, sex and family history while the latter include diabetes mellitus, smoking, dyslipidemia, hypertension and obesity. There is increasing incidence to believe that Asian Indians are at an increased risk of CAD, which cannot be attributed to the common risk factors. Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of the CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrated that Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI-1) and homocysteine levels.[3] The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes i.e. changes in diet, physical inactivity, drug and alcohol intake etc, and increase in prevalence of diabetes mellitus.[4,5] The prevalence of risk factors in a population determines the future burden on health care services and loss of productive years of a particular person. It is not only a health risk for that individual but overall burden on the economy. There are no large scale studies of adequate sample size to evaluate the prevalence rate, risk factor patterns and electrocardiographic changes in Indian populations. This study was planned to evaluate the future risk of CAD in a national level organization. The organization has offices across the entire country (Fig 1). So the study population included subjects from various ethnic groups, staying in varied environments and consuming different varieties of diet. To the best of our knowledge our study is the first such study carried out across India, where the employees are working all over India and belong to different ethnicity spread across the country.

Key words

CAD: coronary artery disease; **BP:** blood pressure; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure; **FPG:** fasting plasma glucose; **PPPG:** post-prandial plasma glucose; **BMI:** body mass index; **LDL-cholesterol:** low-density cholesterol; **HDL-cholesterol:** high density cholesterol; **CVRFs:** cardiovascular risk factors

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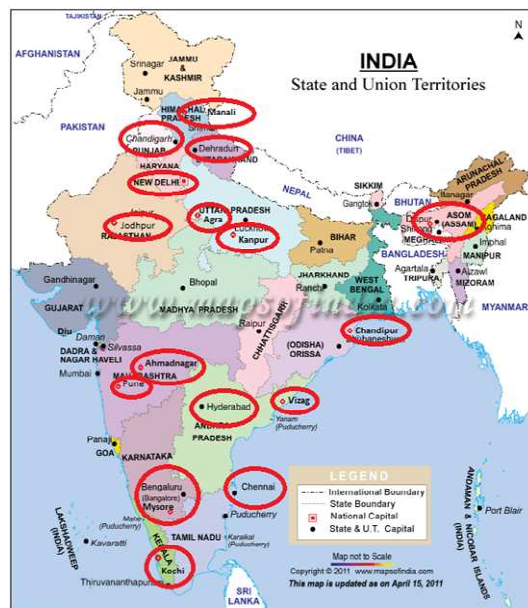


Figure 1: The various labs in country where study was carried out

MATERIAL AND METHODS

Patient Population and Study Design

All the subjects were ~~employees of one national level organisation~~. The subjects of both the sexes were recruited after written informed consent. They fall in the age groups ranging from 20 to 60 years. The recruitment was done across India in 14 states, 20 cities, and, one union territory namely, Delhi (Delhi), Karnataka (Bangalore, Mysore), Andhra Pradesh (Hyderabad, Vishakhapatnam), Maharashtra (Pune, Ambernath, Ahmednagar), Uttar Pradesh (Agra, Kanpur), Rajasthan (Jodhpur), Himachal Pradesh (Manali), Chandigarh, Uttarakhand (Dehradun, Mussourie), Orissa (Chandipur), Assam (Tejpur), Jammu & Kashmir (Leh), Madhya Pradesh (Gwalior), Tamil Nadu (Chennai), Kerala (Kochi). This data collection involved subjects from different states of India like Delhi, Maharashtra, Karnataka, Tamil Nadu, Kerala, UP, Uttarakhand, Himachal Pradesh, Rajasthan, Orissa etc. This is an ongoing study and now is in its phase 2. The patient recruitment was initiated in 2009 and the phase 1 evaluation was completed in 2012. Of the initial 14,000 subjects sampled, 1500 subjects were considered as non-eligible and a sample of 12,500 was subjected to detailed statistical analysis and evaluation. The sample size calculation was not performed as it was an open study where voluntary participation of all employees was encouraged.

Ethical Clearance

The study was approved by the Institutional Ethics Committee of Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi.

Inclusion criteria

a. ~~Employee of the particular organization~~

b. Apparently healthy individual

c. Age 20 – 60 years

d. Both the sexes

Exclusion criterion

a. Known case of coronary artery disease (CAD)

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Assessment process

Participants were asked to attend the Health Center of their respective institution at 8:00 am after an overnight fast. They were asked to continue their medication if any, as usual. A detailed questionnaire was applied by medical personnel prior to clinical measurements and blood collection. The questionnaire recorded information on demographic data, socio-economic and marital status, and several lifestyle factors namely tobacco, alcohol and caffeine consumption, physical activity, family history, disease history, medication use, and family history of premature CAD in first degree relatives (age <55 years in men & <65 years in women). In women, further data regarding reproductive and obstetrical history, oral contraception and hormonal replacement therapy was collected.

Anthropometry and clinical examination including blood pressure measurement was carried out. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5mm using a height gauge. Body mass index (BMI) was defined as weight in Kg/ (height in meters) ².

Blood pressure (BP) and heart rate were measured on the left arm, with an appropriately sized cuff, after at least 10 minutes rest in the seated position using an automated BP instrument. The average of the last two measurements was used for analysis. The subjects diagnosed to have high BP for the first time were called again the next day for BP monitoring before labeling them as hypertensive. In addition, waist and hip circumferences were measured as recommended. Resting ECG was also obtained as a part of evaluation.

Blood samples were collected in the fasting state and 2 hours after 75 grams of oral glucose. Biochemical evaluation of the blood samples included complete blood count, Fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), lipid profile, and liver& kidney function tests. The clinical chemistry tests were performed on fresh blood samples using automatic analyser on the same day. Subjects whose FPG was ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl were diagnosed as fresh cases of Diabetes Mellitus. Other subjects with past history of DM and/or taking medication for the same were also considered as Diabetics.

In the evaluation of Lipid profile the value of Total cholesterol/HDL cholesterol ≥ 4.5 was considered abnormal. Known cases of dyslipidemia and/or those on medication for the same were also included in dyslipidemia risk factor.

Table no. 1. Definitions for different risk factors in the study

Risk factor	Definition
Hypertension	Systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) ≥ 90 mm Hg during the visit and/or presence of anti-hypertensive drug treatment and was considered as known if the subject was aware of this condition.
Diabetes Mellitus	FPG ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl at the time of investigations and/or presence of anti-diabetic drug treatment and was considered as known if the subject was aware of this condition.
Obesity	BMI ≥ 30 kg/ m ²
Overweight	BMI ≥ 25 kg/m ² .

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Hypercholesterolemia	Total blood cholesterol ≥ 200 mg/dl
Decreased High density lipoprotein(HDL) cholesterol	≤ 40 mg/dl
Adverse total cholesterol/High density lipoprotein ratio (Dyslipidemia)	≥ 4.5
Age	>45 years in men; >55 years in women
Sex	Male sex
Family History of CAD	Premature CAD in first degree relatives (<55 years in men & <65 years in women)
Risk factors for CAD	age, sex, family history, diabetes mellitus, smoking, dyslipidemia, hypertension and obesity

The strength of the study is that each participant had one on one interaction with at least one of the project team doctors. Each questionnaire was scrutinised by the doctor. So this added value to the data. In most of the epidemiological studies usually paramedics collect the data.

Statistical Analysis

The final data was recorded on a predesigned Performa and managed in Microsoft access. The data analysis was performed using SPSS 20.0. The values of various parameters are presented as mean and SD (standard Deviation), in absolute numbers and as percentage. Comparison between male and female was done by t-test. Correlation statistics between various risk factors was also computed. Minimum Significance level was set at 0.05.

RESULTS

A total of 14,500 subjects were evaluated in the study. After informed consent, exclusion criteria, clinical & biochemical assessment, complete data of 12,608 cases (Males – 10,642 Females – 1,966) was available for final analysis. Mean age of males was 44.34 ± 10.63 & median age being 47.00 years. Mean age of females was 42.47 ± 10.34 and median age was 44.00 years. Baseline characteristics are shown in Table no. 2 .

Table no.2: Baseline characteristics of the study population (n=12,608)

Parameters \pm SD	MALES (n=10642)	FEMALES (n=1966)	P value
Age	44.34 ± 10.63	42.47 ± 10.34	.000
Height	166.92 ± 6.89	154.74 ± 6.34	.000
Weight	69.36 ± 10.69	62.24 ± 11.30	.001
BMI	24.89 ± 3.58	26.02 ± 4.69	.001
Systolic BP	127.35 ± 16.12	120.05 ± 15.25	.000
Diastolic BP	81.08 ± 10.04	77.05 ± 9.60	.000
FPG	95.91 ± 31.08	93.48 ± 32.10	0.01
PPPG	135.44 ± 56.31	131.86 ± 54.47	.01
Total Cholesterol	186.11 ± 40.56	181.69 ± 36.62	.001
HDL	$42.46 \pm 11.$	46.54 ± 11.36	.001

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Different parameters considered for calculating the risk factors and their results are depicted in Table no. 3.

Table no.3: Percentage (%) of Risk factors in study population (n=12608)

Parameters	Total (n=12608)	MALES (n=10642)	FEMALES (n=1966)	P value
Family H/O CAD	580(4.6%)	460(4.4%)	120(6%)	<.05
Smoking	1471(11.6%)	1469(13.8%)	2(0.1%)	<.001
BMI >25 kg/m ²	6002(47.6%)	4910(46.1%)	1092(55.5%)	
Mean(SD)		27.8 ±3.59	29.17± (3.66)	<.001
BMI 25-30 kg/m ²	4959(39.3%)	4200(39.46%)	759(38.6%)	
Mean(SD)		26.93± 1.31	27.35± 1.44	<.001
BMI ≥30 kg/m ²	1029(8.2%)	700(6.6%)	329(16.7%)	
Mean(SD)		32.78 ± 4.00	33.41± 3.74	<.05
Diabetes Mellitus	2016 (16%)	1766(16.6%)	250 (12.7%)	Ns
Hypertension	2647 (21%)	2383(22.4%)	264(13.4%)	<.001
Dyslipidemia	5755 (45.6%)	5137 (48.27%)	618 (31.4%)	<.001

Family history of premature CAD was present in 4.6% of the study population. The history of CAD in first degree relatives in males was 4.4% and in females was 6% (P value<0.05).

The prevalence of smoking was significantly higher in the men (13.8%) than females (0.1%), p value<0.001.

Out of 12603 study subjects, 6002 (47.6%) had BMI ≥25kg/m² with 4910(46.1%) males and 1092(55.5%) of females, P value<0.001. On further analysis it was observed that 39.46% males and 38.6% of females were overweight with BMI 25-30 kg/m², P value<0.001. The mean BMI of the overweight males was 26.93±1.31 and 27.35±1.44 of females. Obesity with BMI ≥30 kg/m² was present in 6.6% of males with mean BMI of 32.78 ±4 and 16.7% of females with mean BMI of 33.41 ±3.74, p value <0.05.

Overall prevalence of Diabetes was 16% in study population with no significant difference present in male (16.6%) and female (12.7%) subjects. Out of 16% diabetics, 5.6% were fresh diagnosed and 10.4% were known cases of Diabetes Mellitus already on medication.

Out of 10642 male subjects, 2383 (22.4%) were found to have hypertension, whereas out of 1966 female subjects, 264 (13.4%) had high BP, p value<0.001. Overall prevalence of hypertension was 21% in the study subjects. Of these subjects only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study.

The prevalence of dyslipidemia in study population was significantly high with 45.6% of study subjects having high total cholesterol/HDL cholesterol ratio. 48.27% of male subjects and 31.4% females were found to have dyslipidemia (P value<0.001).

Total number of subjects having 2 or more than 2 risk factors for CAD was 9909 (78.6%). 9251 (86.9%) male subjects had 2 or more than 2 risk factors in comparison to 658 (33.46%) females. The most prevalent risk factor in men was dyslipidemia present in 48.27% of males followed by BMI>25

Comment [h8]: The prevalence of hypercholesterolemia in study population was 31.3% with no significant difference in men (32%) and women (27.6%). When the cut off value of low HDL was used as 40 mg/dl for men its prevalence was found to be 37.7% and similarly at a cut off value of low HDL less than 50 mg/dl for women its prevalence was 76%.

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present in 46.1% of males. Whereas in women BMI>25 was most prevalent factor present in 55.5% of women, followed by dyslipidemia in 31.45%.

HDL correlated negatively with FPG, PPPG, and BMI. BMI had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose and total cholesterol. Total cholesterol had a positive correlation with Systolic & diastolic BP, Fasting & PP plasma glucose, BMI (**Table No. 4**).

Table No 4. Correlations by Pearson correlation (2 tailed); (n=12608)

Parameters	BP Systolic	BP Diastolic	FPG	PPPG	Serum Total Cholesterol	Serum HDL	BMI
BP systolic	1	.715(**)	.149(**)	.136(**)	.086(**)	-.011	.190(**)
BP Diastolic	.715(**)	1	.119(**)	.107(**)	.114(**)	-.011	.216(**)
FPG	.149(**)	.119(**)	1	.821(**)	.095(**)	-.054(**)	.099(**)
PPPG	.136(**)	.107(**)	.821(**)	1	.092(**)	-.042(**)	.117(**)
Serum Total Cholesterol	.086(**)	.114(**)	.095(**)	.092(**)	1	.000	.063(**)
Serum HDL Cholesterol	-.011	-.011	-.054(**)	-.042(**)	.000	1	-.068(**)
BMI	.190(**)	.216(**)	.099(**)	.117(**)	.063(**)	-.068(**)	1

** Correlation is significant at the 0.01 level (2-tailed).

Discussion

~~A rise in the prevalence of CAD in the early half of the twentieth century and a subsequent decline in the later half have been well documented in the western countries. However, the scenario has reversed in the developing countries especially in India with a steady escalation in the prevalence of CAD.[3]The CAD burden of India is expected to double by the year 2020, making it the single largest cause of death and 2nd largest cause of disability.[4]~~

The present study deals with finding the prevalence of the risk factors of the CAD, in a national level organization where people from different regions of India work. The employees were of both the sex and age group of 20-60. In the present population of the study, we found that approximately half of the population had dyslipidemia (45.6%) and BMI above 25kg/m² (47.6%). About one fifth of the study population was hypertensive (21%) and one sixth had Diabetes mellitus(16%). 78.6% of the study population had 2 or more than 2 CAD risk factors which indicates that there is a large population who in the near future will develop CAD.

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The results of our study can be compared with the results of Jaipur Heart Watch-5 done by Rajeev Gupta et al on 739 subjects with 451 men and 288 women. In the study, overweight/obesity was present in 46.2% in males and 50.7% of females. [6]Prevalence of Hypertension was 39.5% in males and 24.6% of females. Diabetes was present in 15.5% of males and 10.85 of females. 33% of the males and 32.7% of the females had high cholesterol levels.

Similar results are shown by a study done by Prabhakaran D et al among men working in an industry of Northern India.[7] It showed high serum total cholesterol/HDL ratio in 62%, overweight in 47%, hypertension in 30% and diabetes in 15% of the population. Though in our study 78.6% had 2 or more than 2 risk factors, study by Prabhakaran D has shown 47% of the respondents to have at least 2 of these risk factors.

Another study by Mohan et al in 2008,has shown prevalence of major risk factors for cardiovascular disease as: diabetes 11.9%; hypertension 25.4%; dyslipidemia 40.2%; hypertriglyceridemia 28.3%; overweight (body mass index > or = 23 kg/m2) 60.2%; and metabolic syndrome 34.1%.[8]

Various other studies have also shown similar trends in the Indian population.[9-15] An increasing prevalence of impaired glucose tolerance and diabetes in urban residents of Chennai has been reported by Ramchandran et al.[16]Smoking and low physical activity have been shown to be prevalent in 20-39 year old urban adults by Gupta et al in 2002.[17] Another important independent risk factor for CAD is family H/O of CAD as reported by Goel et al in 2003.[18]

Our study has clearly shown that prevalence of obesity, hypertension, dyslipidemia, diabetes are increasing among the middle class of the Indian population and these modifiable risk factors are responsible for the high prevalence of CAD risk factors. Study has shown direct correlation of increased BMI with dyslipidemia, diabetes and hypertension.CAD has a multi factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as consequence of urbanization may partly explain the escalation of CAD. India is experiencing an epidemiological transition with high rates of urbanization.[19-22] This has led to economic improvement, the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. With the introduction of an era of refined foods, sugar and hydrogenated oils, the traditional high complex carbohydrate, high fibre and low fat diet has been replaced by a diet rich in fats and simple sugars low in dietary fibres.[23]One of the effects of this transition is a shift in the disease spectrum from the communicable to non communicable diseases particularly CAD and Diabetes.[24-26] More importantly the disease is affecting the young Indians i.e. the productive workforce. The incidence of CAD in young Indians is 12-16% which is higher than any other ethnic group. Lack of awareness of the preventable risk factors and ignorance of the disease is also an important factor responsible for the increasing rate of CAD among Indians.[27-32] In the present study out of 21% hypertensive study subject only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study. Similarly, out of 16% diabetics, 5.6% were fresh diagnosed. This shows that awareness and control of hypertension and diabetes was poor in the study population, indicating low detection and poor management of major CAD risk factors.

Prevention and control of the risk factors of CAD can reduce the rate of CAD. It needs changes in the individual as well as changes at the community level. Taking care of modifiable factors such as smoking, increases levels of body fat, too much use of fat and salt in food, sedentary lifestyle together

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with the use of accessible and affordable preventive medicines can definitely make a difference as far as CAD is concerned. Help of the television and media can be utilized to create awareness among the masses. Local Resident Welfare Associations and religious groups can also be empowered to promote healthy lifestyle and exercise among the community.

STRENGTHS & LIMITATIONS OF THE STUDY

- Our study is the first of its type where population was covered across various cities in India. The study population included people of various ethnicities, age groups, and living in different parts of the country.
- There are very few studies across the world where such a large population were studied for the conventional risk factors of CAD.
- The history and clinical examination of the subjects were collected by qualified doctors who interviewed & examined each subject of the study. All the biochemical investigations were performed by the same team using similar kits and evaluation technique.
- The limitation of the study was that out of approximately 26000 working population of this organisation only 14500 gave informed consent to participate in the study. Out of these subjects data could be completed in 12608 subjects and was statistically analysed.
- Because of the limited resources in Phase I we could study and evaluate only the conventional coronary risk factors.

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CONCLUSION

The present study demonstrates high prevalence of CAD risk factors in the Indian population as study population was representative of the national population and it does represent the rising trend of CAD in urban India. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors, promotion of right diet and physical activity and at the same time development of the guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

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We are thankful to Dr RP Tripathi, Director Institute of Nuclear Medicine & Allied Sciences (INMAS) for his constant motivation and support. ~~We are also grateful to the DRDO lab authorities for their cooperation and logistic support.~~ We further extend our thanks to the team in Bangalore i.e. Dr Sripathy G, Dr Jyotsana & Dr Bellubi who provided constant support to the study in regional labs. We are also thankful to Col PJS Bhalla & Lt Col Ashustosh Kansal for the lab work of the study. Dr Naresh Gupta (Professor of Medicine, Maulana Azad Medical College, Delhi) & Dr Shantanu Sengupta (Scientist, Institute of Genomics and Integrative Biology, Delhi) provided continuous guidance in our study.

FUNDINGS

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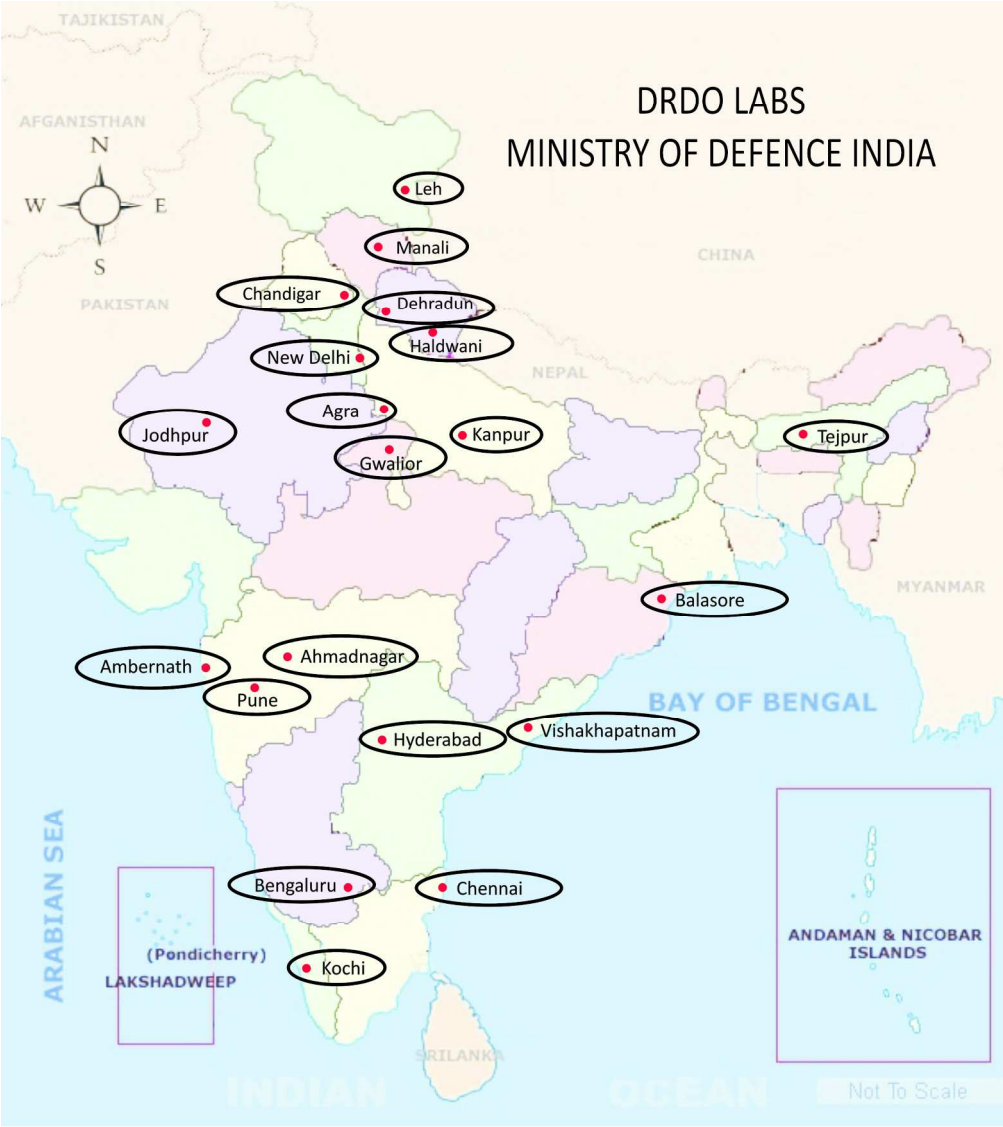
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract [YES] Addressed in manuscript page no 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found [YES] Addressed in manuscript page no 1
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported [YES] Addressed in manuscript page no 2
Objectives	3	State specific objectives, including any prespecified hypotheses [YES] Addressed in manuscript page no 2
Methods		
Study design	4	Present key elements of study design early in the paper [YES] Addressed in manuscript page no 3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [YES] Addressed in manuscript page no 3
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants [YES] Addressed in page no 3 & 4 (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [YES] Addressed in manuscript page no 3 & 4
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [YES] Addressed in manuscript page no 3&4
Bias	9	Describe any efforts to address potential sources of bias [NOT APPLICABLE]
Study size	10	Explain how the study size was arrived at [YES] The employees working in National level organisation were requested to participate in the study. Those people who agreed voluntarily were made a part of study. Out of a total 40000 employees, 14500 agreed to take part in the study. Manuscript Page no 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [YES] The risk factors of CAD were independently studied. Each variable was studied as per the normal range for common clinical parameters.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding [YES] Addressed in manuscript page no 6 (b) Describe any methods used to examine subgroups and interactions [YES]

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Addressed in manuscript page no 6

(c) Explain how missing data were addressed **[YES] The subjects whose data could not be completed for some reason or other were excluded from the study.**

(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed
Case-control study—If applicable, explain how matching of cases and controls was addressed **[NOT APPLICABLE]**
Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy **[YES] Addressed in manuscript page no 6**

(e) Describe any sensitivity analyses

Continued on next page

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Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [YES] Addressed in manuscript page no 6 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [YES] Addressed in manuscript page no 6 (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures [YES] Addressed in manuscript page no 6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [NOT APPLICABLE] (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [NOT APPLICABLE]

Discussion

Key results	18	Summarise key results with reference to study objectives [YES] Addressed in manuscript page no 8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [NIL]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [YES] Addressed in manuscript page no 8 & 9
Generalisability	21	Discuss the generalisability (external validity) of the study results [YES] Addressed in manuscript page no 8 & 9

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [YES] Addressed in manuscript page no 9
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of risk factors for coronary artery disease in urban Indian population

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MANUSCRIPT

Prevalence of risk factors for coronary artery disease in urban Indian population

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ABSTRACT

Objective: The objective of the study was to assess prevalence of risk factors for coronary artery disease (CAD) in government employees posted across India.

Methods: The study population included subjects from government employees posted in different parts of the country {Males (n=10642), Females (n=1966) aged 20 to 60 years} and comprised various ethnic groups, staying in different environmental conditions. The recruitment was done across India in 14 states, 20 cities, and, one union territory. All selected individuals were subjected to detailed questionnaire, medical examinations and anthropometric measurements. Blood samples were collected for blood glucose and serum lipid profile estimation. Resting ECG was also recorded for these subjects. Results were analyzed by using appropriate statistical tools.

Results: The study revealed that the family history of premature CAD was present in 4.6% of the study population. The overall prevalence of diabetes was 16% and out of these, 5.6% were freshly diagnosed while remaining 10.4% were known cases already on medication. Hypertension was present in 21% of subjects. Prevalence of dyslipidemia was significantly high with 45.6% of study subjects having high total cholesterol/HDL ratio. 78.6% subjects had 2 or more risk factors for CAD.

Conclusion: The present study demonstrates high prevalence of CAD risk factors in the Indian urban population. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors to manage individuals at high risk for future CAD.

INTRODUCTION

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Coronary artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries. It is a leading cause of death in India, and its contribution to mortality is rising; deaths due to CAD are expected to double from 1985 to 2015.[1] According to the reports of National Commission on Macroeconomics & Health, there would be 62 million patients with CAD in 2015 in India and of these 23 million would be patients younger than 40 years of age.[2]The prevalence of classical cardiovascular (CV) risk factors (CVRFs) such as hypertension, dyslipidemia, obesity and diabetes varies widely between different countries, and shows some important secular trends.The conventional risk factors of CAD can be divided into non-modifiable and modifiable risk factors. The former include age, sex and family history while the latter include diabetes mellitus, smoking, dyslipidemia, hypertension and obesity. There is increasing incidence to believe that Asian Indians are at an increased risk of CAD, which cannot be attributed to the common risk factors. Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrate that Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI-1) and homocysteine levels.[3]

The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes i.e. changes in diet, physical inactivity, drug and alcohol intake, as well as increase in prevalence of diabetes mellitus.[4,5] The prevalence of risk factors in a population determines the future burden on health care services and loss of productive years of a particular person. It is not only a health risk for that individual but an overall burden on the economy. There are no large scale studies of adequate sample size to evaluate the prevalence rate, risk factor patterns and electrocardiographic changes in Indian populations. The present study was thus planned to evaluate the future risk of CAD in a national level organization. The organization has offices across the entire country (Fig 1). So the study population included subjects from various ethnic groups, staying in varied environments and consuming different varieties of diet. To the best of our knowledge the present study is the first of its kind carried out across India.

Key words

CAD: coronary artery disease; **BP:** blood pressure; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure; **FPG:** fasting plasma glucose; **PPPG:** post-prandial plasma glucose; **BMI:** body mass index; **LDL-cholesterol:** low-density cholesterol; **HDL-cholesterol:** high density cholesterol; **CVRFs:** cardiovascular risk factors

MATERIAL AND METHODS

Patient Population and Study Design

All subjects were civilian government employees posted in various parts of the country. The subjects of both the sexes were recruited after written informed consent. They fall in the age groups ranging from 20 to 60 years. The recruitment was done across India in 14 states, 20 cities, and, one union territory namely, Delhi (Delhi), Karnataka(Bangalore, Mysore), Andhra Pradesh (Hyderabad, Vishakahapatnam), Maharashtra (Pune, Ambernath, Ahmednagar), Uttar Pradesh (Agra, Kanpur), Rajasthan (Jodhpur), Himachal Pradesh (Manali), Chandigarh, Uttrakhand (Dehradun, Mussourie), Orissa (Chandipur), Assam (Tejpur), Jammu & Kashmir (Leh), Madhya Pradesh (Gwalior), Tamil Nadu(Chennai), Kerala (Kochi). This data collection involved subjects from different states of India like Delhi, Maharashtra, Karnataka, Tamil Nadu, Kerala, UP, Uttrakhand, Himachal Pradesh, Rajasthan, and Orissa. The patient recruitment was initiated in 2009 and the phase 1 evaluation was completed in 2012. The sample size calculation was not performed as it was an open study where voluntary participation of all employees was encouraged.

Ethical Clearance

The study was approved by the Institutional Ethics Committee of Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi.

Inclusion criteria

- a. Civilian government employees posted in various parts of the country
- b. Apparently healthy individual
- c. Age 20 – 60 years
- d. Both sexes

Exclusion criterion

- a. Known case of coronary artery disease (CAD)

Assessment process

Participants were asked to visit the health center of their respective institution at 8:00 am after an overnight fast. They were asked to continue their medication if any, as usual. A detailed questionnaire was applied by medical personnel prior to clinical measurements and blood collection. The questionnaire recorded information on demographic data, socio-economic and marital status. Several lifestyle factors were also recorded including tobacco, alcohol and caffeine consumption, physical activity, family history, disease history, medication use, and family history of premature CAD in first degree relatives (age <55 years in men & <65 years in women). In women, further data regarding reproductive and obstetrical history, oral contraception and hormonal replacement therapy was collected.

MANUSCRIPT

For each of the subjects, anthropometric and clinical examination including blood pressure measurement was carried out. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5mm using a height gauge. Body mass index (BMI), defined as weight in Kg/ (height in meters) ² was also calculated.

Blood pressure (BP) and heart rate were measured on the left arm, with an appropriately sized cuff, after at least 10 minutes rest in the seated position using an automated BP instrument. The average of the last two measurements was used for analysis. The subjects diagnosed to have high BP for the first time were called again the next day for BP monitoring before labeling them as hypertensive. Resting ECG was also obtained as a part of evaluation.

Blood samples were collected in the fasting state and 2 hours after 75 grams of oral glucose. Biochemical evaluation of the blood samples included complete blood count, fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), lipid profile, and liver& kidney function tests. The clinical chemistry tests were performed on fresh blood samples using automatic analyser on the same day. Subjects whose FPG was ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl were diagnosed as fresh cases of diabetes mellitus. Other subjects with past history of DM and/or taking medication for the same were also considered as Diabetics.

In the evaluation of lipid profile the value of total cholesterol/HDL cholesterol ≥ 4.5 was considered abnormal. Known cases of dyslipidemia and/or those on medication for the same were also included in dyslipidemia risk factor. Table no. 1 summarises the definitions for different risk factors in the study.

Table no. 1. Definitions for different risk factors in the study

Risk factor	Definition
Hypertension	Systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) ≥ 90 mm Hg during the visit and/or presence of anti-hypertensive drug treatment and was considered as known if the subject was aware of this condition.
Diabetes Mellitus	FPG ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl at the time of investigations and/or presence of anti-diabetic drug treatment and was considered as known if the subject was aware of this condition.
Obesity	BMI ≥ 30 kg/ m ²
Overweight	BMI ≥ 25 kg/m ² .
Hypercholesterolemia	Total blood cholesterol ≥ 200 mg/dl
Decreased High density lipoprotein(HDL) cholesterol	≤ 40 mg/dl
Adverse total cholesterol/High density lipoprotein ratio (Dyslipidemia)	≥ 4.5
Age	>45 years in men; >55 years in women
Sex	Male sex
Family History of CAD	Premature CAD in first degree relatives (<55 years in men & <65 years in women)
Risk factors for CAD	age, sex, family history, diabetes mellitus,

MANUSCRIPT

	smoking, dyslipidemia, hypertension and obesity
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The strength of the study was that each participant had one on one interaction with at least one of the project team doctors. Each questionnaire was scrutinised by the doctor. Therefore this added value to the data. In most of the epidemiological studies usually paramedics collect the data.

Statistical Analysis

The final data was recorded on a predesigned performa and managed in Microsoft access. The data analysis was performed using SPSS 20.0. The values of various parameters are presented as mean and SD (standard deviation), in absolute numbers and as percentage. Comparison between male and female was done by t-test. Correlation statistics between various risk factors was also computed. Minimum significance level was set at 0.05.

RESULTS

A total of 14,500 subjects were evaluated in the study. After informed consent, exclusion criteria, clinical & biochemical assessment, complete data of 12,608 cases (Males – 10,642 Females – 1,966) was available for final analysis. Mean age of males was 44.34±10.63 & median age being 47.00 years. Mean age of females was 42.47±10.34 and median age was 44.00 years. Baseline characteristics are shown in **Table no. 2**.

Table no.2: Baseline characteristics of the study population (n=12,608)

Parameters ± SD	MALES (n=10642)	FEMALES (n=1966)	P value
Age	44.34±10.63	42.47±10.34	.000
Height	166.92±6.89	154.74±6.34	.000
Weight	69.36±10.69	62.24±11.30	.001
BMI	24.89±3.58	26.02±4.69	.001
Systolic BP	127.35±16.12	120.05±15.25	.000
Diastolic BP	81.08±10.04	77.05±9.60	.000
FPG	95.91±31.08	93.48±32.10	0.01
PPPG	135.44±56.31	131.86±54.47	.01
Total Cholesterol	186.11±40.56	181.69±36.62	.001
HDL	42.46±11.55	46.54±11.36	.001

Different parameters considered for calculating the risk factors and their results are depicted in **Table no. 3**.

Table no.3: Percentage (%) of Risk factors in study population (n=12608)

Parameters	Total (n=12608)	MALES (n=10642)	FEMALES (n=1966)	P value
Family H/O CAD	580(4.6%)	460(4.4%)	120(6%)	<.05
Smoking	1471(11.6%)	1469(13.8%)	2(0.1%)	<.001
BMI >25 kg/m ²	6002(47.6%)	4910(46.1%)	1092(55.5%)	
Mean(SD)		27.8 ±3.59	29.17± (3.66)	<.001
BMI 25-30 kg/m ²	4959(39.3%)	4200(39.46%)	759(38.6%)	
Mean(SD)		26.93± 1.31	27.35± 1.44	<.001
BMI ≥30 kg/m ²	1029(8.2%)	700(6.6%)	329(16.7%)	
Mean(SD)		32.78 ± 4.00	33.41± 3.74	<.05
Diabetes Mellitus	2016 (16%)	1766(16.6%)	250 (12.7%)	Ns
Hypertension	2647 (21%)	2383(22.4%)	264(13.4%)	<.001
Dyslipidemia	5755 (45.6%)	5137 (48.27%)	618 (31.4%)	<.001

Family history of premature CAD was present in 4.6% of the study population. The history of CAD in first degree relatives in males was 4.4% and in females was 6% (P value<0.05). The prevalence of smoking was significantly higher in the men (13.8%) than females (0.1%), p value<0.001.

Out of 12603 study subjects, 6002 (47.6%) had BMI ≥25kg/m² with 4910(46.1%) males and 1092(55.5%) of females, P value<0.001. On further analysis it was observed that 39.46% males and 38.6% of females were overweight with BMI 25-30 kg/m²,P value<0.001. The mean BMI of the overweight males was 26.93±1.31 and 27.35±1.44 for females. Obesity with BMI ≥30 kg/m² was present in 6.6% of males with mean BMI of 32.78 ±4 and 16.7% of females with mean BMI of 33.41 ±3.74, p value <0.05.

Overall prevalence of diabetes was 16% in study population with no significant difference present in male (16.6%) and female (12.7%) subjects. Out of 16% diabetics, 5.6% were fresh diagnosed and 10.4% were known cases of diabetes mellitus already on medication.

Out of 10642 male subjects, 2383 (22.4%) were found to have hypertension, whereas out of 1966 female subjects, 264 (13.4%) had high BP, p value<0.001. Overall prevalence of hypertension was

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21% in the study subjects. Of these subjects only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study.

The prevalence of dyslipidemia in study population was significantly high with 45.6% of study subjects having high total cholesterol/HDL cholesterol ratio. 48.27% of male subjects and 31.4% females were found to have dyslipidemia (P value<0.001). The prevalence of hypercholesterolemia in study population was 31.3% with no significant difference in men (32%) and women (27.6%). When the cut off value of low HDL was used as 40 mg/dl for men its prevalence was found to be 37.7% and similarly at a cut off value of low HDL less than 50 mg/dl for women its prevalence was 76%.

The study population was divided into four groups according to their age. Subjects of age 20 to 30 years (N=1885), 30 to 40 years (N=2724), 40 to 50 years (N=3604) and 50 to 60 years (N=4395) were categorized as group I, group II, group III, and group IV respectively.

The mean level of total cholesterol in these age groups was group I - 174.2 mg/dl, II -182.5 mg/dl, III -188.2 mg/dl IV -189.7 mg/dl. These levels were significantly higher in group II as compared to group I (p value <0.05). Significant difference was found when we compared group III and group II (p value <0.05), however there was no significant difference in these values when groups III and IV were compared. Mean HDL Cholesterol levels in these age groups were group I – 43.79 mg/dl, II – 42.53 mg/dl, III – 42.80 mg/dl, IV – 43.37 mg/dl. No significant difference was seen in the levels of HDL cholesterol among these age groups.

Total number of subjects having 2 or more than 2 risk factors for CAD was 9909 (78.6%). 9251 (86.9%) male subjects had 2 or more than 2 risk factors in comparison to 658 (33.46%) females. The most prevalent risk factor in men was dyslipidemia present in 48.27% of males followed by BMI>25 present in 46.1% of males. Whereas in women BMI>25 was most prevalent factor present in 55.5% of women, followed by dyslipidemia in 31.45%.

HDL correlated negatively with FPG, PPPG, and BMI. BMI had a positive correlation with systolic & diastolic BP, fasting & PP plasma glucose and total cholesterol. Total cholesterol had a positive correlation with systolic & diastolic BP, fasting & PP plasma glucose, BMI (Table No. 4).

Table No 4. Correlations among risk factors by Pearson Correlation (2 tailed); (n=12608)

Parameters	BP Systolic	BP Diastolic	FPG	PPPG	Serum Total Cholesterol	Serum HDL	BMI
BP systolic	1	.715(**)	.149(**)	.136(**)	.086(**)	-.011	.190(**)
BP Diastolic	.715(**)	1	.119(**)	.107(**)	.114(**)	-.011	.216(**)
FPG	.149(**)	.119(**)	1	.821(**)	.095(**)	-.054(**)	.099(**)
PPPG	.136(**)	.107(**)	.821(**)	1	.092(**)	-.042(**)	.117(**)
Serum Total Cholesterol	.086(**)	.114(**)	.095(**)	.092(**)	1	.000	.063(**)
Serum HDL Cholesterol	-.011	-.011	-.054(**)	-.042(**)	.000	1	-.068(**)

MANUSCRIPT

BMI	.190(**)	.216(**)	.099(**)	.117(**)	.063(**)	-.068(**)	1
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** Correlation is significant at the 0.01 level (2-tailed).

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Discussion

The present study dealt with finding prevalence of risk factors of CAD, in a national level organization where people from different regions of India work. The employees were of both the sex and age group of 20-60. In the present population of the study, it was found that approximately half of the population had dyslipidemia (45.6%) and BMI above 25kg/m² (47.6%). About one fifth of the study population was hypertensive (21%) and one sixth had diabetes mellitus(16%). 78.6% of the study population had 2 or more than 2 CAD risk factors which indicates that there is a large population who in the near future will develop CAD.

The results of the present study can be compared with the results of Jaipur Heart Watch-5 done by Rajeev Gupta et al on 739 subjects with 451 men and 288 women. In the study, overweight/obesity was present in 46.2% in males and 50.7% of females. [6]Prevalence of Hypertension was 39.5% in males and 24.6% of females. Diabetes was present in 15.5% of males and 10.85 of females. 33% of the males and 32.7% of the females had high cholesterol levels.

Similar results are shown by a study done by Prabhakaran D et al among men working in an industry of Northern India.[7] It showed high serum total cholesterol/HDL ratio in 62%, overweight in 47%, hypertension in 30% and diabetes in 15% of the population. Though in the present study 78.6% had 2 or more than 2 risk factors, study by Prabhakaran D has shown 47% of the respondents to have at least 2 of these risk factors.

Another study by Mohan et al in 2008,has shown prevalence of major risk factors for cardiovascular disease as: diabetes 11.9%; hypertension 25.4%; dyslipidemia 40.2%; hypertriglyceridemia 28.3%; overweight (body mass index ≥ 23 kg/m²) 60.2%; and metabolic syndrome 34.1%.[8]

Various other studies have also shown similar trends in the Indian population.[9-15] An increasing prevalence of impaired glucose tolerance and diabetes in urban residents of Chennai has been reported by Ramchandran et al.[16]Smoking and low physical activity have been shown to be prevalent in 20-39 year old urban adults by Gupta et al in 2002.[17] Another important independent risk factor for CAD is family H/O of CAD as reported by Goel et al in 2003.[18]

Our study has clearly shown that prevalence of obesity, hypertension, dyslipidemia, diabetes are increasing among the middle class of the Indian population and these modifiable risk factors are responsible for the high prevalence of CAD risk factors. Study has shown direct correlation of increased BMI with dyslipidemia, diabetes and hypertension.CAD has a multi factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as consequence of urbanization may partly explain the escalation of CAD. India is experiencing an epidemiological transition with high rates of urbanization.[19-22] This has led to economic improvement, the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. With the introduction of an era of refined foods, sugar and hydrogenated oils, the traditional high complex carbohydrate, high fibre and low fat diet has been replaced by a diet rich in fats and simple sugars low in dietary fibres.[23] One of the effects of this transition is a shift in the disease spectrum from the communicable to non communicable diseases particularly CAD and diabetes.[24-26] More importantly the disease is affecting the young Indians i.e. the productive workforce. The incidence of CAD in young Indians is 12-16% which is higher than any other ethnic group. Lack of awareness of the preventable risk factors and ignorance of the disease

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is also an important factor responsible for the increasing rate of CAD among Indians.[27-32] In the present study out of 21% hypertensive study subjects only 4.76% were aware of the condition and were on medication while the remaining and 16.22% were identified during the study. Similarly, out of 16% diabetics, 5.6% were fresh diagnosed. This shows that awareness and control of hypertension and diabetes was poor in the study population, indicating low detection and poor management of major CAD risk factors.

Prevention and control of the risk factors of CAD can reduce the rate of CAD. It needs changes in the individual as well as changes at the community level. Taking care of modifiable factors such as smoking, increased levels of body fat, too much use of fat and salt in food, sedentary lifestyle together with the use of accessible and affordable preventive medicines can definitely make a difference as far as CAD is concerned. Help of television and other media can be utilized to create awareness among the masses. Local resident welfare associations and religious groups can also be empowered to promote healthy lifestyle and exercise among the community.

STRENGTHS & LIMITATIONS OF THE STUDY

- Our study is the first of its type where population was covered across various cities in India. The study population included people of various ethnicities, age groups, and living in different parts of the country.
- The history and clinical examination of the subjects were collected by qualified doctors who interviewed & examined each subject of the study. All the biochemical investigations were performed by the same team using similar kits and evaluation technique.
- The limitation of the study was that out of approximately 26000 working population of this organisation only 14500 gave informed consent to participate in the study. Out of these subjects data could be completed in 12608 subjects and was statistically analysed.
- Because of the limited resources in Phase I we could study and evaluate only the conventional coronary risk factors.

CONCLUSION

The present study demonstrates high prevalence of CAD risk factors in the Indian population as study population was representative of the national population and it does represent the rising trend of CAD in urban India. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors, promotion of right diet and physical activity and at the same time development of guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

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MANUSCRIPT

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CONTRIBUTORSHIP STATEMENT

Sekhri T1* Principal investigator of the study, Kanwar RS1 Co principal investigator of the study and also involved in medical evaluation and manuscript writing, Wilfred R1 medical evaluation of the study subjects and data compilation, Chugh P1 medical evaluation of the study subjects and data compilation,, Chhillar M1 medical evaluation of the study subjects and data compilation,, Aggarwal R1 medical evaluation of the study subjects and data compilation,, Sharma YK2 statistical evaluation and analysis of study population, Sethi J1 dietary evaluation and data compilation, Sundriyal J1 laboratory sample analysis, Bhadra K1 laboratory sample analysis, Singh S1 laboratory sample analysis laboratory sample analysis Rautela N1 laboratory sample analysis, Tekchand1 laboratory sample analysis, Singh M1 laboratory sample analysis, Singh SK1 laboratory sample analysis.

COMPETING INTERESTS

There are no competing interests.

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DATA SHARING

Extra data of this project can be accessed by emailing Dr Tarun Sekhri, corresponding author at tarunsekhri@yahoo.com.

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Prevalence of risk factors for coronary artery disease in urban Indian population – DRDO Health Study

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ABSTRACT

Objective: The objective of the study was to assess ~~the~~ prevalence of risk factors for coronary artery disease (CAD) in defense services workers posted across ~~the country~~ India.

Methods: The study population included subjects from ministry of defence employees posted in different parts of the country {Males (n=10642), Females (n=1966) aged 20 to 60 years} and comprised ~~of~~ various ethnic groups, staying in different environmental conditions. The recruitment was done across India in 14 states, 20 cities, and, one union territory. All ~~the following selected~~ individuals were subjected to detailed questionnaire, medical examinations and anthropometric measurements. Blood samples were collected for blood glucose and serum lipid profile estimation. Resting ECG was also recorded for these subjects. Results were analyzed by using appropriate statistical tools.

Results: The study revealed that the family history of premature CAD was present in 4.6% of the study population. The overall prevalence of ~~D~~diabetes was 16% and out of ~~16% diabetesthese~~, 5.6% were freshly diagnosed ~~and while remaining~~ 10.4% were known cases ~~of Diabetes Mellitus~~ already on medication. Hypertension was present in 21% of subjects. Prevalence of dyslipidemia was significantly high with 45.6% of study subjects having high total cholesterol/HDL ratio. 78.6% ~~S~~subjects had 2 or more risk factors for CAD.

Conclusion: The present study demonstrates high prevalence of CAD risk factors in the Indian urban population. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors to manage individuals at high risk for future CAD.

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INTRODUCTION

Coronary artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries. It is a leading cause of death in India, and its contribution to mortality is rising; deaths due to CAD are expected to double from 1985 to 2015.[1] According to the reports of National Commission on Macroeconomics & Health, there would be 62 million patients with CAD in 2015 in India and of these 23 million would be patients younger than 40 years of age.[2] The prevalence of classical cardiovascular (CV) risk factors (CVRFs) such as hypertension, dyslipidemia, obesity and diabetes varies widely between different countries, and shows some important secular trends. The conventional risk factors of CAD can be divided into non-modifiable and modifiable risk factors. The former include age, sex and family history while the latter include diabetes mellitus, smoking, dyslipidemia, hypertension and obesity. There is increasing incidence to believe that Asian Indians are at an increased risk of CAD, which cannot be attributed to the common risk factors. Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of the CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrated that Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI-1) and homocysteine levels.[3]

The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes i.e. changes in diet, physical inactivity, drug and alcohol intake etc, as well as and increase in prevalence of diabetes mellitus.[4,5] The prevalence of risk factors in a population determines the future burden on health care services and loss of productive years of a particular person. It is not only a health risk for that individual but an overall burden on the economy. There are no large scale studies of adequate sample size to evaluate the prevalence rate, risk factor patterns and electrocardiographic changes in Indian populations. The present study was thus planned to evaluate the future risk of CAD in a national level organization. The organization has offices across the entire country (Fig 1). So the study population included subjects from various ethnic groups, staying in varied environments and consuming different varieties of diet. To the best of our knowledge the present study is the first of its kind such study carried out across India, where the employees are working all over India and belong to different ethnicity spread across the country.

Key words

CAD: coronary artery disease; **BP:** blood pressure; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure; **FPG:** fasting plasma glucose; **PPPG:** post-prandial plasma glucose; **BMI:** body mass index; **LDL-cholesterol:** low-density cholesterol; **HDL-cholesterol:** high density cholesterol; **CVRFs:** cardiovascular risk factors

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Figure 1: The various labs in country where study was carried out

MATERIAL AND METHODS

Patient Population and Study Design

All the subjects were civilian employees posted in various parts of the country under ministry of defence. The subjects of both the sexes were recruited after written informed consent. They fall in the age groups ranging from 20 to 60 years. The recruitment was done across India in 14 states, 20 cities, and, one union territory namely, Delhi (Delhi), Karnataka(Bangalore, Mysore), Andhra Pradesh (Hyderabad, Vishakahapatnam), Maharashtra (Pune, Ambernath, Ahmednagar), Uttar Pradesh (Agra, Kanpur), Rajasthan (Jodhpur), Himachal Pradesh (Manali), Chandigarh, Uttarakhand (Dehradun, Mussourie), Orissa (Chandipur), Assam (Tejpur), Jammu & Kashmir (Leh), Madhya Pradesh (Gwalior), Tamil Nadu(Chennai), Kerala (Kochi). This data collection involved subjects from different states of India like Delhi, Maharashtra, Karnataka, Tamil Nadu, Kerala, UP, Uttarakhand, Himachal Pradesh, Rajasthan, and Orissa-etc. This is an ongoing study and now is in its phase 2. The patient recruitment was initiated in 2009 and the phase 1 evaluation was completed in 2012. Of the initial 14,000 subjects sampled, 1500 subjects were considered as non-eligible and a sample of 12,500 was subjected to detailed statistical analysis and evaluation. The sample size calculation was not performed as it was an open study where voluntary participation of all employees was encouraged.

Ethical Clearance

The study was approved by the Institutional Ethics Committee of Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi.

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Inclusion criteria

- a. Civilian employees posted in various parts of the country under ministry of defence
- b. Apparently healthy individual
- c. Age 20 – 60 years
- d. Both ~~the~~ sexes

Exclusion criterion

- a. Known case of coronary artery disease (CAD)

Assessment process

Participants were asked to ~~visit-attend~~ the ~~H~~health ~~C~~center of their respective institution at 8:00 am after an overnight fast. They were asked to continue their medication if any, as usual. A detailed questionnaire was applied by medical personnel prior to clinical measurements and blood collection. The questionnaire recorded information on demographic data, socio-economic and marital status, ~~and~~ ~~several~~ lifestyle factors ~~were also recorded including-namely~~ tobacco, alcohol and caffeine consumption, physical activity, family history, disease history, medication use, and family history of premature CAD in first degree relatives (age <55 years in men & <65 years in women). In women, further data regarding reproductive and obstetrical history, oral contraception and hormonal replacement therapy was collected.

~~For each of the subjects, a~~Anthropometry~~ic~~ and clinical examination including blood pressure measurement was carried out. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5mm using a height gauge. Body mass index (BMI), ~~was~~ defined as weight in Kg/ (height in meters) ² ~~was also calculated.~~

Blood pressure (BP) and heart rate were measured on the left arm, with an appropriately sized cuff, after at least 10 minutes rest in the seated position using an automated BP instrument. The average of the last two measurements was used for analysis. The subjects diagnosed to have high BP for the first time were called again the next day for BP monitoring before labeling them as hypertensive. ~~In addition, waist and hip circumferences were measured as recommended.~~ Resting ECG was also obtained as a part of evaluation.

Blood samples were collected in the fasting state and 2 hours after 75 grams of oral glucose. Biochemical evaluation of the blood samples included complete blood count, ~~F~~fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), lipid profile, and liver& kidney function tests. The clinical chemistry tests were performed on fresh blood samples using automatic analyser on the same day. Subjects whose FPG was ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl were diagnosed as fresh cases of ~~D~~diabetes ~~M~~mellitus. Other subjects with past history of DM and/or taking medication for the same were also considered as Diabetics.

In the evaluation of ~~L~~lipid profile the value of ~~T~~total cholesterol/HDL cholesterol ≥ 4.5 was considered abnormal. Known cases of dyslipidemia and/or those on medication for the same were also included in dyslipidemia risk factor.

Table no. 1. Definitions for different risk factors in the study

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Risk factor	Definition
Hypertension	Systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) ≥ 90 mm Hg during the visit and/or presence of anti-hypertensive drug treatment and was considered as known if the subject was aware of this condition.
Diabetes Mellitus	FPG ≥ 126 mg/dl and/or PPPG ≥ 200 mg/dl at the time of investigations and/or presence of anti-diabetic drug treatment and was considered as known if the subject was aware of this condition.
Obesity	BMI ≥ 30 kg/ m ²
Overweight	BMI ≥ 25 kg/m ² .
Hypercholesterolemia	Total blood cholesterol ≥ 200 mg/dl
Decreased High density lipoprotein(HDL) cholesterol	≤ 40 mg/dl
Adverse total cholesterol/High density lipoprotein ratio (Dyslipidemia)	≥ 4.5
Age	>45 years in men; >55 years in women
Sex	Male sex
Family History of CAD	Premature CAD in first degree relatives (<55 years in men & <65 years in women)
Risk factors for CAD	age, sex, family history, diabetes mellitus, smoking, dyslipidemia, hypertension and obesity

The strength of the study ~~was~~ that each participant had one on one interaction with at least one of the project team doctors. Each questionnaire was scrutinised by the doctor. ~~Therefore So +~~ this added value to the data. In most of the epidemiological studies usually paramedics collect the data.

Statistical Analysis

The final data was recorded on a predesigned ~~p~~Performa and managed in Microsoft access. The data analysis was performed using SPSS 20.0. The values of various parameters are presented as mean and SD (standard ~~d~~Deviation), in absolute numbers and as percentage. Comparison between male and female was done by t-test. Correlation statistics between various risk factors was also computed. Minimum ~~s~~Significance level was set at 0.05.

RESULTS

A total of 14,500 subjects were evaluated in the study. After informed consent, exclusion criteria, clinical & biochemical assessment, complete data of 12,608 cases (Males – 10,642 Females – 1,966) was available for final analysis. Mean age of males was 44.34 ± 10.63 & median age being 47.00 years. Mean age of females was 42.47 ± 10.34 and median age was 44.00 years. Baseline characteristics are shown in Table no. 2 .

Table no.2: Baseline characteristics of the study population (n=12,608)

Parameters \pm SD	MALES (n=10642)	FEMALES (n=1966)	P value
Age	44.34 ± 10.63	42.47 ± 10.34	.000
Height	166.92 ± 6.89	154.74 ± 6.34	.000
Weight	69.36 ± 10.69	62.24 ± 11.30	.001
BMI	24.89 ± 3.58	26.02 ± 4.69	.001
Systolic BP	127.35 ± 16	120.05 ± 15.25	.000

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Diastolic BP	81.08±10.04	77.05±9.60	.000
FPG	95.91±31.08	93.48±32.10	0.01
PPPG	135.44±56.31	131.86±54.47	.01
Total Cholesterol	186.11±40.56	181.69±36.62	.001
HDL	42.46±11.55	46.54±11.36	.001

Different parameters considered for calculating the risk factors and their results are depicted in Table no. 3.

Table no.3: Percentage (%) of Risk factors in study population (n=12608)

Parameters	Total (n=12608)	MALES (n=10642)	FEMALES (n=1966)	P value
Family H/O CAD	580(4.6%)	460(4.4%)	120(6%)	<.05
Smoking	1471(11.6%)	1469(13.8%)	2(0.1%)	<.001
BMI >25 kg/m ²	6002(47.6%)	4910(46.1%)	1092(55.5%)	
Mean(SD)		27.8 ±3.59	29.17± (3.66)	<.001
BMI 25-30 kg/m ²	4959(39.3%)	4200(39.46%)	759(38.6%)	
Mean(SD)		26.93± 1.31	27.35± 1.44	<.001
BMI ≥30 kg/m ²	1029(8.2%)	700(6.6%)	329(16.7%)	
Mean(SD)		32.78 ± 4.00	33.41± 3.74	<.05
Diabetes Mellitus	2016 (16%)	1766(16.6%)	250 (12.7%)	Ns
Hypertension	2647 (21%)	2383(22.4%)	264(13.4%)	<.001
Dyslipidemia	5755 (45.6%)	5137 (48.27%)	618 (31.4%)	<.001

Family history of premature CAD was present in 4.6% of the study population. The history of CAD in first degree relatives in males was 4.4% and in females was 6% (P value<0.05).

The prevalence of smoking was significantly higher in the men (13.8%) than females (0.1%), p value<0.001.

Out of 12603 study subjects, 6002 (47.6%) had BMI ≥25kg/m² with 4910(46.1%) males and 1092(55.5%) of females, P value<0.001. On further analysis it was observed that 39.46% males and 38.6% of females were overweight with BMI 25-30 kg/m², P value<0.001. The mean BMI of the overweight males was 26.93±1.31 and 27.35±1.44 for females. Obesity with BMI ≥30 kg/m² was present in 6.6% of males with mean BMI of 32.78 ±4 and 16.7% of females with mean BMI of 33.41 ±3.74, p value <0.05.

Overall prevalence of diabetes was 16% in study population with no significant difference present in male (16.6%) and female (12.7%) subjects. Out of 16% diabetics, 5.6% were fresh diagnosed and 10.4% were known cases of diabetes mellitus already on medication.

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Out of 10642 male subjects, 2383 (22.4%) were found to have hypertension, whereas out of 1966 female subjects, 264 (13.4%) had high BP, p value<0.001. Overall prevalence of hypertension was 21% in the study subjects. Of these subjects only 4.76% were aware of the condition and were on medication and 16.22% were identified during the study.

The prevalence of dyslipidemia in study population was significantly high with 45.6% of study subjects having high total cholesterol/HDL cholesterol ratio. 48.27% of male subjects and 31.4% females were found to have dyslipidemia (P value<0.001). The prevalence of hypercholesterolemia in study population was 31.3% with no significant difference in men (32%) and women (27.6%). When the cut off value of low HDL was used as 40 mg/dl for men its prevalence was found to be 37.7% and similarly at a cut off value of low HDL less than 50 mg/dl for women its prevalence was 76%.

The study population was divided into four groups according to their age. Subjects of age 20 to 30 years (N=1885), 30 to 40 years (N=2724), 40 to 50 years (N=3604) and 50 to 60 years (N=4395) were categorized as group I, group II, group III, and group IV respectively.

The mean level of total cholesterol in these age groups was group I - 174.2 mg/dl, II -182.5 mg/dl, III -188.2 mg/dl IV -189.7 mg/dl. These levels were significantly higher in group II as compared to group I (p value <0.05). Significant difference was found when we compared group III and group II (p value <0.05), however there was no significant difference in these values when groups III and IV were compared. Mean HDL Cholesterol levels in these age groups were group I – 43.79 mg/dl, II – 42.53 mg/dl, III – 42.80 mg/dl, IV – 43.37 mg/dl. No significant difference was seen in the levels of HDL cholesterol among these age groups.

Total number of subjects having 2 or more than 2 risk factors for CAD was 9909 (78.6%).9251 (86.9%) male subjects had 2 or more than 2 risk factors in comparison to658 (33.46%)females.The most prevalent risk factor in men was dyslipidemia present in 48.27% of males followed by BMI>25 present in 46.1% of males. Whereas in women BMI>25 was most prevalent factor present in 55.5% of women, followed by dyslipidemia in 31.45%.

HDL correlated negatively with FPG, PPPG, and BMI. BMI had a positive correlation with sSystolic & diastolic BP, Ffasting & PP plasma glucose and total cholesterol. Total cholesterol had a positive correlation with Ssystolic & diastolic BP, Ffasting & PP plasma glucose, BMI (Table No. 4).

Table No 4. Correlations among risk factors by Pearson eCorrelation (2 tailed); (n=12608)

Parameters	BP Systolic	BP Diastolic	FPG	PPPG	Serum Total Cholesterol	Serum HDL	BMI
BP systolic	1	.715(**)	.149(**)	.136(**)	.086(**)	-.011	.190(**)
BP Diastolic	.715(**)	1	.119(**)	.107(**)	.114(**)	-.011	.216(**)
FPG	.149(**)	.119(**)	1	.821(**)	.095(**)	-.054(**)	.099(**)
PPPG	.136(**)	.107(**)	.821(**)	1	.092(**)	-.042(**)	.117(**)
Serum Total Cholesterol	.086(**)	.114(**)	.095(**)	.092(**)	1	.000	.063(**)

8

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Serum HDL Cholesterol	-.011	-.011	-.054(**)	-.042(**)	.000	1	-.068(**)
BMI	.190(**)	.216(**)	.099(**)	.117(**)	.063(**)	-.068(**)	1

** Correlation is significant at the 0.01 level (2-tailed).

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Discussion

The present study dealt with finding the prevalence of the risk factors of the CAD, in a national level organization where people from different regions of India work. The employees were of both the sex and age group of 20-60. In the present population of the study, it was found that approximately half of the population had dyslipidemia (45.6%) and BMI above 25kg/m² (47.6%). About one fifth of the study population was hypertensive (21%) and one sixth had Diabetes mellitus(16%). 78.6% of the study population had 2 or more than 2 CAD risk factors which indicates that there is a large population who in the near future will develop CAD.

The results of the present study can be compared with the results of Jaipur Heart Watch-5 done by Rajeev Gupta et al on 739 subjects with 451 men and 288 women. In the study, overweight/obesity was present in 46.2% in males and 50.7% of females. [6]Prevalence of Hypertension was 39.5% in males and 24.6% of females. Diabetes was present in 15.5% of males and 10.85 of females. 33% of the males and 32.7% of the females had high cholesterol levels.

Similar results are shown by a study done by Prabhakaran D et al among men working in an industry of Northern India.[7] It showed high serum total cholesterol/HDL ratio in 62%, overweight in 47%, hypertension in 30% and diabetes in 15% of the population. Though in the present study 78.6% had 2 or more than 2 risk factors, study by Prabhakaran D has shown 47% of the respondents to have at least 2 of these risk factors.

Another study by Mohan et al in 2008,has shown prevalence of major risk factors for cardiovascular disease as: diabetes 11.9%; hypertension 25.4%; dyslipidemia 40.2%; hypertriglyceridemia 28.3%; overweight (body mass index > or = 23 kg/m2) 60.2%; and metabolic syndrome 34.1%.[8]

Various other studies have also shown similar trends in the Indian population.[9-15] An increasing prevalence of impaired glucose tolerance and diabetes in urban residents of Chennai has been reported by Ramchandran et al.[16]Smoking and low physical activity have been shown to be prevalent in 20-39 year old urban adults by Gupta et al in 2002.[17] Another important independent risk factor for CAD is family H/O of CAD as reported by Goel et al in 2003.[18]

Our study has clearly shown that prevalence of obesity, hypertension, dyslipidemia, diabetes are increasing among the middle class of the Indian population and these modifiable risk factors are responsible for the high prevalence of CAD risk factors. Study has shown direct correlation of increased BMI with dyslipidemia, diabetes and hypertension.CAD has a multi factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as consequence of urbanization may partly explain the escalation of CAD. India is experiencing an epidemiological transition with high rates of urbanization.[19-22] This has led to economic improvement, the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. With the introduction of an era of refined foods, sugar and hydrogenated oils, the traditional high complex carbohydrate, high fibre and low fat diet has been replaced by a diet rich in fats and simple sugars low in dietary fibres.[23] One of the effects of this transition is a shift in the disease spectrum from the communicable to non communicable diseases particularly CAD and Diabetes.[24-26] More importantly the disease is affecting the young Indians i.e. the productive workforce. The incidence of CAD in young Indians is 12-16% which is higher than any other ethnic group. Lack of awareness of the preventable risk factors and ignorance of the disease

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is also an important factor responsible for the increasing rate of CAD among Indians.[27-32] In the present study out of 21% hypertensive study subjects only 4.76% were aware of the condition and were on medication while the remaining- and 16.22% were identified during the study. Similarly, out of 16% diabetics, 5.6% were fresh diagnosed. This shows that awareness and control of hypertension and diabetes was poor in the study population, indicating low detection and poor management of major CAD risk factors.

Prevention and control of the risk factors of CAD can reduce the rate of CAD. It needs changes in the individual as well as changes at the community level. Taking care of modifiable factors such as smoking, increased levels of body fat, too much use of fat and salt in food, sedentary lifestyle together with the use of accessible and affordable preventive medicines can definitely make a difference as far as CAD is concerned. Help of the television and other media can be utilized to create awareness among the masses. Local Resident Welfare Associations and religious groups can also be empowered to promote healthy lifestyle and exercise among the community.

STRENGTHS & LIMITATIONS OF THE STUDY

- Our study is the first of its type where population was covered across various cities in India. The study population included people of various ethnicities, age groups, and living in different parts of the country.
- ~~There are very few studies across the world where such a large population were studied for the conventional risk factors of CAD.~~
- The history and clinical examination of the subjects were collected by qualified doctors who interviewed & examined each subject of the study. All the biochemical investigations were performed by the same team using similar kits and evaluation technique.
- The limitation of the study was that out of approximately 26000 working population of this organisation only 14500 gave informed consent to participate in the study. Out of these subjects data could be completed in 12608 subjects and was statistically analysed.
- Because of the limited resources in Phase I we could study and evaluate only the conventional coronary risk factors.

CONCLUSION

The present study demonstrates high prevalence of CAD risk factors in the Indian population as study population was representative of the national population and it does represent the rising trend of CAD in urban India. The incidence of CAD is likely to increase further because of rapid urbanization and its accompanying lifestyle changes. Therefore, there is an immediate need to initiate awareness among the masses about these risk factors, promotion of right diet and physical activity and at the same time development of the guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

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Thanks are also due to each of our subjects for their consent and time.

CONTRIBUTORSHIP STATEMENT

Sekhri T1* Principal investigator of the study, Kanwar RS1 Co principal investigator of the study and also involved in medical evaluation and manuscript writing, Wilfred R1 medical evaluation of the study subjects and data compilation, Chugh P1 medical evaluation of the study subjects and data compilation,, Chhillar M1 medical evaluation of the study subjects and data compilation,, Aggarwal R1 medical evaluation of the study subjects and data compilation,, Sharma YK2 statistical evaluation and analysis of study population, Sethi J1 dietary evaluation and data compilation, Sundriyal J1 laboratory sample analysis, Bhadra K1 laboratory sample analysis, Singh S1 laboratory sample analysis laboratory sample analysis Rautela N1 laboratory sample analysis, Tekchand1 laboratory sample analysis, Singh M1 laboratory sample analysis, Singh SK1 laboratory sample analysis.

COMPETING INTERESTS

There are no competing interests.

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DATA SHARING

Extra data of this project can be accessed by emailing Dr Tarun Sekhri, corresponding author at tarunsekhri@yahoo.com.

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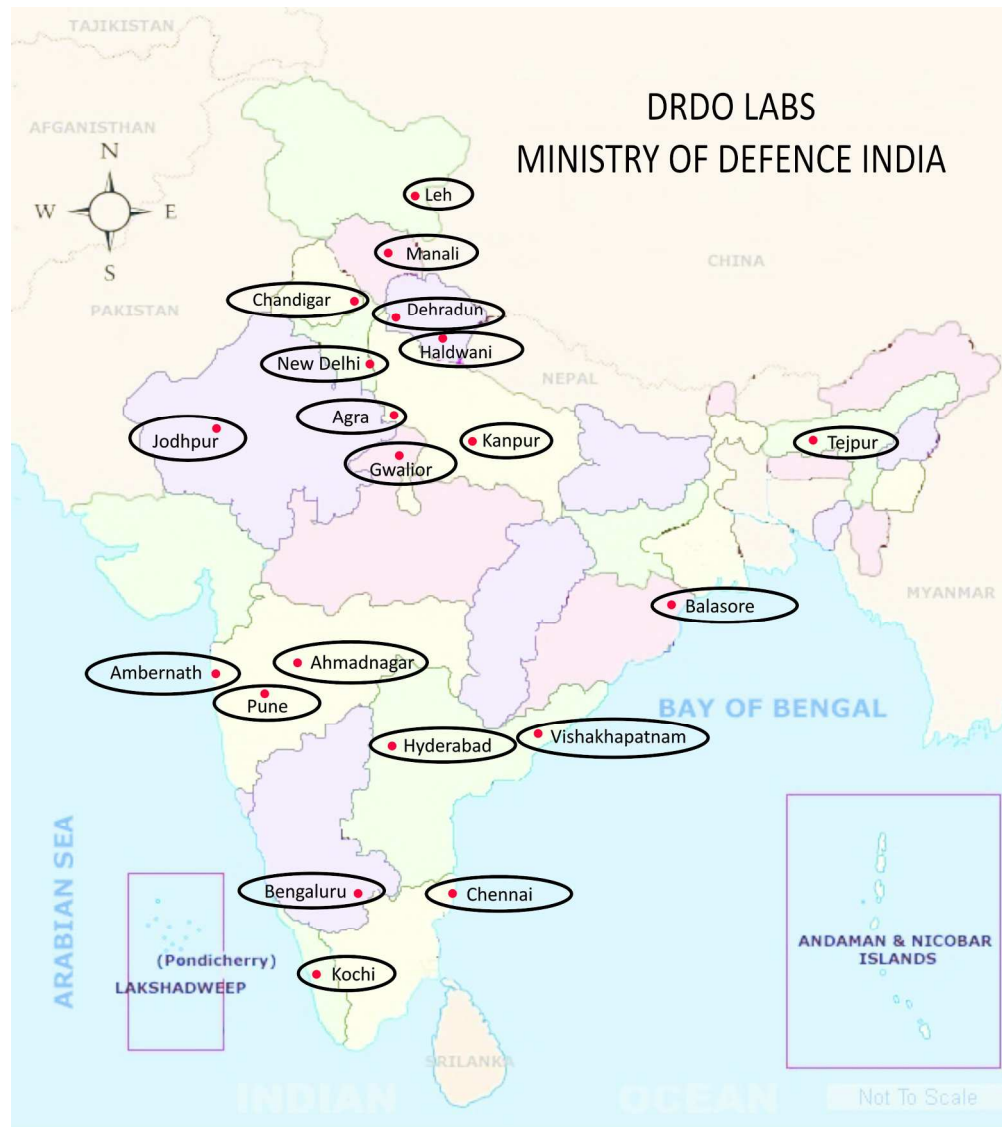
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract [YES] Addressed in manuscript page no 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found [YES] Addressed in manuscript page no 1
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported[YES] Addressed in manuscript page no 2
Objectives	3	State specific objectives, including any prespecified hypotheses [YES] Addressed in manuscript page no 2
Methods		
Study design	4	Present key elements of study design early in the paper [YES] Addressed in manuscript page no 3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [YES] Addressed in manuscript page no 3
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants [YES] Addressed in page no 3 & 4 (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [YES] Addressed in manuscript page no 3 & 4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [YES] Addressed in manuscript page no 3&4
Bias	9	Describe any efforts to address potential sources of bias [NOT APPLICABLE]
Study size	10	Explain how the study size was arrived at [YES] The employees working in National level organisation were requested to participate in the study. Those people who agreed voluntarily were made a part of study. Out of a total 40000 employees, 14500 agreed to take part in the study. Manuscript Page no 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [YES] The risk factors of CAD were independently studied. Each variable was studied as per the normal range for common clinical parameters.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding [YES] Addressed in manuscript page no 6 (b) Describe any methods used to examine subgroups and interactions [YES]

Addressed in manuscript page no 6

(c) Explain how missing data were addressed [YES] **The subjects whose data could not be completed for some reason or other were excluded from the study.**

(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed

Case-control study—If applicable, explain how matching of cases and controls was addressed [NOT APPLICABLE]

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy [YES] **Addressed in manuscript page no 6**

(e) Describe any sensitivity analyses

Continued on next page

For peer review only

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [YES] Addressed in manuscript page no 6 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [YES] Addressed in manuscript page no 6 (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures [YES] Addressed in manuscript page no 6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [NOT APPLICABLE] (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [NOT APPLICABLE]

Discussion

Key results	18	Summarise key results with reference to study objectives [YES] Addressed in manuscript page no 8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [NIL]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [YES] Addressed in manuscript page no 8 & 9
Generalisability	21	Discuss the generalisability (external validity) of the study results [YES] Addressed in manuscript page no 8 & 9

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [YES] Addressed in manuscript page no 9
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.